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CHAGAS' DISEASE.

A Critical Review.

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The present position of knowledge on the mode of transmission of Chagas' disease has been discussed by Hoare (1934) in a recent volume of this *Bulletin*. Whilst the geographical distribution of infected bugs has not yet been fully investigated there seems little doubt that they are widely distributed in the American continent between the latitudes 35°S. and 30°N. They have been found all over the south-eastern portion of Brazil and Uruguay, except in the coastal zone, in Paraguay, in all the provinces in the northern portion of the Argentine, in Chili, Peru, Venezuela, Panama, Salvador, Guatemala, and as far north as the southern portions of California and Arizona, U.S.A.

In view of this wide distribution of infected vectors, it is remarkable that it is still a matter of considerable doubt how far South American trypanosomiasis is a disease of grave significance. The number of human beings hitherto found to be actually infected with the trypanosome is remarkably small. The only district from which any considerable number of cases has been recorded is that of the State of Minas Geraes in Brazil. It was here that Chagas first discovered the disease in 1909: in 1916 he published an account of the 29 acute cases of the disease which he had up to that time met with in infants and young children living in that State. All these children had parasites in the blood, and of 23 which he was able to follow no less than 11 died. Villela and Bicalho (1923) working in the same State record that they recovered the trypanosome from 5 of 19 supposed chronic cases of the disease by inoculation of the blood into guineapigs. Whilst it is impossible from the voluminous and diffuse literature to discover even approximately in how many individuals from Minas Geraes the parasite has actually been discovered, there seems to be no reason to doubt that there is in this State a considerable focus of the infection, but that, probably owing to the firm conviction of the Brazilian workers that endemic goitre, which is so common in that part of Brazil, is merely one of the manifestations of the trypanosomal infection, the pathogenic effects of Chagas' disease in Minas Geraes have been considerably overestimated.

The only other Brazilian State in which definite instances of human infection have been found is that of São Paulo, from which 4 cases have so far been recorded.

Outside Brazil the total number of individuals in whom trypanosomes have been discovered is remarkably small ; the reviewer has been able to find records of only 113 cases. These cases were scattered over an immense area. The total number found in the Argentine is 83*, and these were distributed throughout all the provinces in the northern portion of the country, except Los Andes and Misiones. Two cases have been recorded from Peru, 4 from Venezuela, 19 from Panama, 2 from Salvador and 3 from Guatemala. So far the trypanosome has not been found in human beings in Uruguay, Equador, Paraguay, Mexico, or in southern California and Arizona, U.S.A., although infected bugs have been discovered in all these countries. Details of the distribution of the cases in whom a definite diagnosis has been made by the discovery of the trypanosome are given in the accompanying table.

Table showing the geographical distribution of individuals in whom T. cruzi *has been found.*

Country and Province	No. of cases described	Authority	Age and sex
Brazil.			
Minas Geraes	Many	Chagas (1916) Villela and Bicalho (1923) Villela (1930), Dias (1934) etc.	29 cases : children mostly under 2 years Many cases
São Paulo	4	Carini and Maciel (1914) Villela (1918) Bayma (1914)	1 case : ♀ 10 years 1 case : child 2 cases : child and adult
Venezuela.			
Guárico ...	4	Tejera (1919) Torrealba (1934)	3 cases : ♂ 9 months ; ♂ 2 years† ; ♀ 17 years 1 case : ♀ child
Salvador ...	2	Segovia (1914) (1922)	2 cases : ♀ 30 years ; ♂ 45 years
Peru ...	2	Escomel (1919) Noguchi (1924)	1 case : ♂ 40 years 1 case : *T. cruzi* found in blood culture from supposed case of yellow fever
Guatemala ...	3	Reichenow (1934)	3 cases : ♀ 14 months ; ♂ 14 months ; ♂ 18 months
Panama ...	19	Miller (1931) Clark and Dunn (1932) Clark (1934). Personal communication to DeCoursey DeCoursey (1935) Johnson and de Rivas (1936)	3 cases : ♀ 18 months ; ♀ 2 years ; ♂ 6 months 2 cases : ♂ child ; ♀ 10 years 7 cases : 6 years ; 36 years ; 10 years ; 25 years ; 50 years ; 18 years ; 74 years 1 case : 3½ months† 6 cases : ♂ 3 months† ; ♂ 3 years† ; ♀ 14 years ; ♂ 1½ years ; 28 years ; 14 years

* In a recent paper Mazza (1936*c*) states that the total number of cases found by the Misión de Estudios de Pat. Reg. Argentina between 1932 and 1st August, 1936, is 109 ; a number of these cases have not yet been published.

Country and Province	No. of cases described	Authority	Age and sex
Argentine.			
Catamarca	12	Geoghegan (1928)	2 cases ; 9 months ; child
		Geoghegan (1929)	1 case : ♂ 7 months†
		Geoghegan (1933)	2 cases ; ♂ 3½ months ; ♂ 8 months
		Mazza and Ruchelli (1934)	2 cases : ♀ 5 years ; ♀ 9 years
		Mazza and Ruchelli (1936)*	4 cases : ♀ 7 years ; ♂ 2 years ; ♂ 2½ years ; ♀ 32 years
		Mazza and Herrera (1936)*	1 case : ♂ 35 years
Chaco ...	7	Romaña (1934)	1 case : ♀ 2½ years
		Mazza and Govi (1935)	1 case : ♂ 4 years
		Mazza and Palamedi (1936)	1 case : ♂ 1½ years
		Mazza and Valle (1936)	1 case : ♀ 6 months
		Mazza and Corsi (1936)	1 case : ♂ 3 years
		Mazza and Corsi (1936)*	2 cases : ♀ 11 years ; ♂ 2 years
Córdoba ...	5	Zuccarini and Oyarzabal (1933)	1 case : ♂ 8 years
		Villegas (1934)	2 cases : ♀ 23 years ; ♀ 3 years
		Mazza and Belmont Sánchez (1936)*	1 case : ♂ 6 years
		Mazza (1936)*	1 case : ♂ 9 years
Corrientes	2	Mazza, Benítez and Janzi (1936)	1 case : ♀ 6 years
		Mazza and Benítez (1936)	1 case : ♂ 18 years
Entre Ríos	2	Cáceres and Izaguirre (1935)	1 case : ♂ 5 years
		Mazza, Idelsohn and Parcerisa (1936)	1 case : ♀ 3 years
Formoso	1	Mazza (1936)	1 case : ♂ 4 years
Jujuy ...	12	Mühlens, Dios, Petrocchi and Zuccarini (1925)	1 case : ♀ 8 years
		Mazza (1926)	1 case : ♀ 27 years
		Mazza (1934)	2 cases ; ♂ 4 years ; ♀ 6 months
		Mazza and Almaraz (1934)	1 case : ♀ 5 years
		Mazza (1934)	1 case : adult
		Mazza (1936)*	1 case : ♀ 2 years
		Mazza (1936)*	3 cases : ♂ 1 7/12 years ; ♀ 7 years ; ♂ 8 years
		Mazza (1936)*	1 case : ♀ 35 years
		Mazza and Chacon (1936)*	1 case : ♂ 3 years
La Rioja	1	Fitte (1935) Mazza and Catalán (1936)*	1 case : ♂ 1 1/12 years
Mendoza ...	3	Mazza, Germinal and Basso (1935)	1 case : ♀ 9 months
		Basso, G. and Basso, R. (1936)*	2 cases : ♂ 9 years ; ♂ 4 years

Country and Province	No. of cases described	Authority	Age and sex
Argentine (cont.)			
Salta ...	3	Niño (1928)	1 case : ♀ 38 years
		Mazza and Mainoli (1936)	1 case : ♂ 4 years
		Mazza and Cornejo (1936)*	1 case : ♂ 37 years
San Juan ...	2	Mazza and Nastri de Fischer (1935)	2 cases : ♀ 6 years ; ♀ 11 months†
Santa Fé	20	Romaña (1934)	1 case : ♂ 8 years
		Mazza and Romaña (1934)	1 case : ♀ 1 year†
		Romaña (1934)	3 cases : ♂ 1½ years ; ♂ 10 years ; ♀ 4 years
		Mazza, Romaña and Parma (1935)	1 case : ♂ 2½ years†
		Romaña (1935)	2 cases : ♂ 9 years ; ♂ 4 years
		Mazza, Romaña and Parma (1936)	1 case : ♂ 8 years
		Mazza, Romaña and Zambra (1936)	1 case : ♂ 7 years
		Mazza and Schreiber (1936)*	3 cases : ♀ 6 years ; ♀ 7 years ; ♂ 2½ years
		Romaña and Klemensiewicz (1936)*	2 cases : ♂ 12 years ; ♀ 2 years
		Romaña (1936)*	4 cases : ♂ 52 days ; ♀ 7 years ; ♂ 4 years ; ♂ 12 years†
		Romaña and Romero Cereijo (1936)*	1 case : ♀ 5 years
Santiago del Estero	10	Mazza and Guerrini (1934)	2 cases : ♀ 4 years ; ♀ 14 years
		Raimondi and Canal Feijoó (1934)	1 case : ♂ 8 years
		Mazza and Olle (1936)	2 cases : ♀ 5 years ; ♂ 33 years
		Canal Feijoó (1936)*	2 cases : ♂ 19 years ; ♂ 26 days
		Mazza and Guerrini (1936)*	1 case : ♀ 7 years
		Mazza and Argañaráz (1936)*	2 cases : ♀ 3 months ; ♂ 8 months
Tucumán	3	Mühlens, Dios, Petrocchi and Zuccarini (1925)	1 case : ♀ 5 months
		Dios, Zuccarini and Oyarzabal (1925)	1 case : ♂ 4 years
		Borzone and Coda (1925)	1 case : child

* The references marked thus relate to papers which are to be found in Novena Reunión Pat. Reg. Soc. Argentina.

† The cases marked thus died.

N.B.—In a recent article Mazza (1936*c*) states that the total number of infected cases found by the Misión de Estudios de Patologia Regional Argentina between 1932 and 1st August, 1936 is 109. Some of these cases have not yet been recorded. These 109 cases were distributed as follows :—Entre Rios 2, Corrientes 2, Santa Fé 27, Formoso 1, Chaco 10, Santiago del Estero 14, Salta 4, Jujuy 10, Córdoba 2, Catamarca 10, La Rioja 3, San Juan 2, and Mendoza 22. The total number of deaths observed among these cases is 7, viz., 4 in Santa Fé, 1 in Santiago del Estero, 1 in San Juan and 1 in Mendoza.

Pathology.—The earliest accounts of the pathology of Chagas' disease are those of CHAGAS (1911) and of VIANNA (1911), who based their descriptions on the examination of the tissues of the Minas Geraes cases. Some years later TORRES (1917) gave a description of the lesions in the heart found in 4 of the 29 acute cases of the disease described by CHAGAS (1916). References to post-mortem findings are scattered throughout the subsequent papers of Chagas and other Brazilian writers, but whether they relate to cases already described, or even to Chagas' disease at all, it is often impossible to decide. Many years later, CROWELL (1923), who spent 4 years at the Oswaldo Cruz Institute, where he had the opportunity of examining the tissues of a number of Chagas' cases, gave a detailed account of the pathological findings in an acute case of the disease. He states in this article that in later papers he will deal with the pathology of the chronic form in some of its aspects, but, so far as the reviewer has been able to ascertain, these papers have not yet appeared. It is interesting to note that CHAGAS and VILLELA (1922), in their paper giving information of 62 chronic cases stated to be suffering from the cardiac form of the disease, record that in 5 of them CROWELL discovered characteristic lesions in the heart: this is referred to again later.

Goitre is extremely common in the part of Brazil from which the cases came, and CHAGAS and his colleagues firmly believed that *Trypanosoma cruzi* was the cause of this condition, which they designated "Parasitic thyroiditis." There has, however, recently been accumulated a considerable mass of evidence, which will be referred to later, indicating that this hypothesis is untenable, and that CHAGAS was actually dealing with two distinct diseases, *viz.*, a trypanosome infection and endemic goitre; in fact, there now seems little doubt that in many of CHAGAS's cases the trypanosomal infection was superimposed on epidemic goitre. This confusion of two distinct diseases makes it extremely difficult from a consideration of the Minas Geraes cases alone to unravel how much of the pathology and clinical signs ascribed by Chagas to the trypanosomal infection are really due to this disease.

Among the 117 cases, which have hitherto been diagnosed by discovery of the parasite in places other than Minas Geraes (4 from São Paulo and 113 from countries other than Brazil), only 7 deaths have been recorded (*vide* Table). One of the Santa Fé cases (MAZZA and ROMAÑA, 1934) was discovered at post-mortem to have died from broncho-pneumonia and pneumococcal meningitis, but showed typical cardiac lesions; the remaining 6 cases appear to have died of the disease, and autopsies were performed on 4 of them. As, fortunately, in some of these, particularly in the Panama cases (DECOURSEY, 1935, and JOHNSON and DE RIVAS, 1936), the complication of endemic goitre can be excluded, it is possible now to reach a fairly definite impression regarding the pathology of the acute stage of Chagas' disease.

Broadly speaking, it may be said that the pathological changes caused by the trypanosome consist in degeneration of the invaded cells and in a cellular infiltration and eventually in a fibrosis of the affected tissues. Whilst in acute cases parasites have been discovered in almost every organ in the body, the outstanding lesions are usually found in the heart, brain, and liver.

Heart.—The heart is usually enlarged, and there is an excess of pericardial fluid of a yellowish or yellowish-green colour, sometimes containing a few fibrous flakes. Microscopic examination of the heart

muscle shows the most pronounced changes. There is evidence of a diffuse myocarditis ; between the muscle fibres there is an extensive infiltration of lymphocytes, plasmocytes, macrophages, and round cells. The muscle fibres themselves are widely separated from one another, and some of them show fragmentation and hyaline degeneration. Large nests of parasites are usually to be found either in the muscle fibres themselves or in the large monoculear cells and lymphocytes lying between the muscle fibres.

The epicardium and endocardium may likewise show in places cellular infiltration and nests of parasites.

Skeletal muscles.—The muscles appear to be one of the seats of election for the multiplication of the parasites. The changes found in the voluntary muscles are essentially similar to those which occur in the heart. Between the muscle fibres are small foci of cellular infiltration, and parasites can be found both in the muscle fibres themselves and also in large mononuclear cells lying between the muscle fibres.

Brain.—Certain cases showed pronounced cerebral changes : the brain and meninges were congested and oedematous, and scattered throughout the substance of the brain were numerous small inflammatory foci. On section these lesions were seen to consist of collections of neuroglia cells mixed with mononuclear cells. These foci were not related to the blood vessels and occurred in all parts of the brain. Parasites may be found in the neuroglia cells and in the large mononuclear cells of these inflammatory foci, and in isolated cells outside the foci.

Liver.—Enlargement of the liver appears to be a very common phenomenon. On section the organ shows parenchymatous changes with extreme fatty degeneration. The presence of parasites in the liver is not a common occurrence, but they have been found in the Kupffer cells.

Spleen.—This organ is usually somewhat enlarged and congested, but studies on the histology of the spleen in this disease are complicated by malaria. Parasites are not commonly found in the spleen, but they have been recorded from at least one case (Mazza, Romaña and Parma, 1935).

Lymphatic glands.—The lymphatic glands are enlarged, and histological examination shows congestion, lymphoid hyperplasia, mononuclear cell production and phagocytosis, with red cell destruction and a destruction of other elements that are phagocytosed. Trypanosomes have apparently not been found in this situation.

Other sites in which parasites have been found at post-mortem examination of acute cases are the thyroid, suprarenals, ovaries, and testicles.

Whilst the cardiac lesions mentioned above appear to be constantly found in young children who have died in the acute stage of the disease, it is of importance to inquire what happens in the majority of cases when the lesions are not sufficiently severe to result in death. Two recent papers—one by Mazza and Romaña (1934) and the other by these authors and Parma (1935)—throw some light on the matter. Mazza and Romaña describe the conditions found in the heart of a child 12 months old, who died of bronchopneumonia 5 weeks after the commencement of an acute attack of the disease. The heart muscle fibres were normal, but the interstitial tissue showed an intense infiltration by monocytes which separated the muscle fibres one from the

other. There was also a hyperplasia of connective tissue and a commencing fibrosis. No parasites were found, but in certain places in the fibrous connective tissue a few large cells with alveolar cytoplasm and polymorphic nucleus were seen. These cells, which the authors call polycaryocytes, probably correspond to the giant cells found by TORRES (1917) in experimental animals, and are believed to be the site of parasites which had disappeared. In a later paper (1935) MAZZA and ROMAÑA record the results of further examination of sections of the heart of this case, and state that in one of these polycaryocytes they found a large nest of parasites. Very similar changes were found by MAZZA, ROMAÑA and PARMA (1935) in a child 2⅓ years old, who died suddenly from convulsions a month after the commencement of an acute attack of the disease. These cases suggest that, if the heart lesions are not sufficiently severe to kill the child in the acute stage of the disease, the infiltrated areas undergo fibrotic changes.

The subject is of importance because, as will be mentioned later, CHAGAS and other writers attach great importance to the cardiac form of the disease in chronic cases. In one paper already referred to CHAGAS and VILLELA (1922) give clinical details of no less than 62 such cases in individuals between 11 and 54 years of age. Five of these patients died, and it is briefly recorded that in their hearts CROWELL found characteristic lesions, with parasites in one of the cases. Unfortunately it is not stated what these characteristic lesions were, or how they can be recognized in the absence of parasites. Possibly they represent a more advanced stage of the interstitial fibrosis referred to by MAZZA, ROMAÑA and PARMA. EV. CHAGAS (1935*c*) in a recent paper states that in sections of the hearts of chronic cardiac cases there is hyperplasia of connective tissue and fibrosis with parenchymatous degeneration. He adds that the parasites tend to migrate to neighbouring regions, so that adjacent to extensive fibrotic areas one may find acute lesions characterized by an intensive inflammatory cellular exudate with degenerating muscle fibres and sometimes parasitic agglomerations. EV. CHAGAS believes that as time goes on the infection tends to become attenuated owing to the defensive mechanism of the host, and consequently if re-infection is not constantly taking place the infection may come to an end. He considers that it is this fact which makes the trypanosomes so difficult to find in chronic cases.

Symptomatology.—Whilst many of those in whose blood the trypanosome is found exhibit no sign of disease and give no history of recent illness, beyond possibly a mild febrile disturbance associated with some facial oedema and adenitis, there seems little doubt that in infants and young children the infection is associated with an acute febrile disturbance, which, however, varies considerably in severity in different cases ; as a rule, the younger the child the more severe are the symptoms.

In infants and young children the illness commences with a febrile disturbance, the temperature in severe cases rising to 104°F. A very common early sign is swelling of the eyelids and face. The oedema, which is at times accompanied by conjunctivitis, is firm, elastic and painless, and may be so marked that the eye cannot be opened. It is usually unilateral, and is probably to be ascribed to the bite of the infected bug. Experimentally (EV. CHAGAS, 1935*a*), it has been shown that man and animals can be infected by placing the excreta of infected bugs upon the conjunctiva, and it is believed that the face and eyelids

or conjunctiva constitute the usual portals of entry of the virus. The bugs bite the closed eyelids or the neighbouring regions of the face, and the child inoculates the wound or the conjunctiva by rubbing in the infected excreta. Ev. CHAGAS (1935*b*) states that the incubation period in his experimentally infected human beings was 10 to 12 days.

Study of the literature seems to afford abundant evidence that in severe cases the oedema may spread widely and involve the extremities and even the whole body. CHAGAS (1911 and 1916) attaches great importance to this subcutaneous swelling as a frequent early sign in acute cases of the disease. He states that the swelling begins in the face and rapidly becomes generalized ; that when the flagellates disappear from the blood and the temperature becomes normal the oedema, as a rule, subsides, but that in certain severe cases a marked oedema persists for an indefinite period. CHAGAS describes the swelling as a hard oedema of elastic consistency, which does not pit on pressure. He believes that it is due to a myxoedematous infiltration of the subcutaneous tissue, and that it is to be explained by a specific action of the parasite or of its toxins on the thyroid gland. He points out that his patients were infants of a few months of age, or at most in the first years of life, and in perfect health. ROMAÑA (1935), MAZZA (1936*b*), DIAS (1936*b*) and other Argentine observers similarly draw attention to oedema of the face as an important early sign in the acute stage of the disease. ROMAÑA observed the condition in 8 of 9 Argentine cases between 1 and 10 years of age. Some of these lived in districts where endemic goitre is unknown. ROMAÑA remarks that the oedema may spread widely, and that the legs and arms may become involved ; when the febrile disturbance subsides the swelling disappears. DECOURSEY (1935) in his account of the first fatal case of Chagas' disease observed in Panama mentions that the patient, a black baby, 3 months old, became ill with fever and swelling of the face and extremities about 5 days before death occurred. At post-mortem DECOURSEY found that " the thyroid was firm, symmetric, and of normal size and colour ; it presented no microscopic lesions." ESCOMEL (1919), writing of the case of Chagas' disease which he found in Peru—a man of 40 years of age who came to consult him for gonorrhoea—states that his attention was drawn to the hard oedema of the eyelids, the limbs, and the rest of the body ; it was this fact, in conjunction with the absence of signs of renal disease, which caused him to search for the trypanosomes. In all of the three patients (aged 9 months, 2 years, and 17 years, respectively) found by TEJERA (1919) in Venezuela oedema of the face and body was pronounced. Of the three mild cases (aged 14 months, 19 months, and 14 months, respectively) discovered by REICHENOW (1934) in Guatemala one exhibited slight oedema of the face.

There seems no reason to doubt, therefore, that oedema, usually involving the face and sometimes spreading widely over the body, is a very constant early sign of the disease. Whether, however, CHAGAS's explanation of the phenomenon, *viz.*, that it is due to the action of toxins on the thyroid gland, is correct, is, as will be mentioned later, a matter of considerable doubt. The transient oedemas of the early stages of African trypanosomiasis are well known, and are usually assumed to be due to a general toxic action of the parasite ; it is possible that the more pronounced oedema characteristic of the early stage of Chagas' disease is a closely related phenomenon.

Associated with the oedema is an adenitis ; the pre-auricular, submaxillary, and cervical glands are frequently involved, as also are the

inguinal and axillary glands. There is progressive anaemia, and the pulse is frequent, the tachycardia being independent of the temperature. The liver and spleen are enlarged, but the latter is probably often due in part to concomitant malaria. In severe cases various nervous symptoms, such as irritability, convulsions, twitchings, and clonic contractions, have been described. As a rule, the cardiac signs in the acute stages are ill-defined, and indicated solely by the enfeeblement of the organ and by tachycardia, without the marked alterations of rhythm which are said to be characteristic of certain chronic cases.

The acute stage of the disease is of short duration. Among the severe cases, which are met with, as a rule, in very young children, a considerable proportion of deaths have been recorded. CHAGAS (1916) gave an account of 29 acute cases found in Minas Geraes. Of these, 15 were in the first year of life, 11 in the second and 1 in the third and fourth years. No less than 11 of the patients died, 8 of whom were under 1 year of age. Seven of the 19 cases hitherto discovered in Panama were under 3 years of age, and three of them died. One of the two acute cases discovered by TEJERA in Venezuela died; this was a child 2 years of age. Twenty-six of the 83 cases diagnosed in Argentina by the discovery of the parasites were under 3 years of age, and 4 of the 5 cases recorded as having died belong to this group: one of these presumably died of bronchopneumonia and pneumococcal meningitis, but characteristic lesions due to *T. cruzi* were found in the myocardium; the other 4 (2 of whom were in the first year of life, one $2\frac{1}{3}$ years old, and the other 12 years of age) may well have died of the disease.

In those cases which survive the acute stage the temperature usually returns to normal within a few weeks, and with the fall of temperature the trypanosomes disappear from the blood and the oedema and other signs subside. Sometimes, however, the febrile disturbance, with its accompanying signs, is prolonged for several months. MAZZA and BELMONT SÁNCHEZ (1936), for example, give details of the case of a boy aged 6 years in whom the febrile disturbance was prolonged from the end of July 1935 to December 1935; parasites were found in the blood on a number of occasions during the whole of this period.

CHAGAS (1916) believed, however, that spontaneous cure does not occur, and that those who escape death in the acute period all pass on into the chronic stage of the disease, the manifestations of which are due to multiplication of the parasite in the internal organs. He also held that the disease may present itself from the first as a chronic infection, without having passed through the acute phase. It has already been mentioned that in older children and adults the infection usually produces no immediate symptoms beyond possibly a mild febrile disturbance. Many of the infections were discovered only as the result of systematic examination of the blood of a large number of individuals, or accidentally during examination of the blood for malaria. MÜHLENS and his collaborators (1925) inoculated 6 general paralytics with the trypanosome, but only 3 became infected and these exhibited practically no symptoms. A number of patients suffering from malignant disease were experimentally infected by EV. CHAGAS (1934–1936), and here again the symptoms were mild.

In his earlier papers CHAGAS (1911) described in great detail various chronic forms of the disease, which he divided into 5 clinical groups, *viz.*, a pseudomyxoedematous form, a myxoedematous form, a cardiac form, a nervous form, and a chronic form with subacute manifestations. Although in later papers (1916) he somewhat modified his views, he

remained convinced that the disease was responsible for various forms of myocardial disease, of nervous disease, of infantilism, of hypothyroidism and goitre met with so commonly in Minas Geraes. CHAGAS attributes these various conditions to the ravages wrought by the trypanosome in such organs as the heart, brain, thyroid, testis, and endocrine glands. If CHAGAS's views are correct, then the disease which bears his name is unquestionably of very great pathological significance. Recent work, however, has raised considerable doubt whether many of the conditions included by CHAGAS among the chronic forms of his disease are in any way the result of infection with *Trypanosoma cruzi.*

KRAUS and ROSENBUSCH and MAGGIO (1915 and 1917) were the first to impugn the validity of CHAGAS's views regarding the chronic form of the disease, and the whole subject was again reviewed by KRAUS (1926) ten years later. These authors point out that, excluding the chronic cardiac cases, the symptomatology of the chronic forms of the disease described by Chagas—*viz.*, goitre, derangement of the intelligence which may lead to idiocy, defects of speech and aphasia, paralysis, cerebral diplegia, myxoedema and infantilism—has a marked analogy with that of endemic goitre and cretinism in Europe. They recall that CHAGAS's work was done in a hilly region of Brazil (Minas Geraes), where, according to MUNK (1923), 75 per cent. of the native inhabitants have goitre, and where a cretin, dwarf or paralytic occurs in every family ; no cases of the disease are recorded from the Brazilian plains, where infected bugs are also found. As the result of their own investigations in the Argentine, KRAUS and his colleagues found infected bugs in the provinces of Salta and Jujuy, Tucumán, Santiago del Estero, La Rioja, Catamarca, Córdoba, Santa Fé, Buenos Aires and La Pampa. The facts that on the one hand in certain of these provinces (Córdoba, La Pampa and Buenos Aires) infected bugs were common, but goitre, which, according to CHAGAS, is one of the cardinal symptoms of the disease, could not be discovered, and that on the other hand in Northern Provinces, such as Salta and Jujuy, where infected bugs also occur, goitre and cretinism were endemic, led them to look for Chagas' disease in the Argentine. Most of the investigations were carried out in Salta and Jujuy, where endemic goitre and cretinism is seen in all stages of development—aphasia, paralysis, defects of intelligence, etc. In many places 60 to 70 per cent. of the natives are goitrous and nearly one-third of the inhabitants are cretinous, so that in almost every house a cretin can be found. ROSENBUSCH examined blood of newly-born children and of adults both by means of thick films and inoculation of guineapigs, but never succeeded in finding trypanosomes. ROSENBUSCH furthermore made the very interesting observations that, although generally speaking endemic goitre and cretinism are widespread in Salta, there is one valley (Valle Calchacie) in which, notwithstanding the fact that the houses are overrun with infected bugs, neither goitre nor cretinism is demonstrable. A further interesting fact which in KRAUS's opinion also tells against the view that the goitre and cretinism of the Argentine are chronic Chagas' disease, is the occurrence of goitre and cretinism in the domestic animals of the endemic areas. KRAUS was able to produce goitre in rats in Buenos Aires by giving them water brought from endemic areas. After reviewing the literature, KRAUS reached the conclusion that CHAGAS's dictum—where there are infected Triatoma there is *Trypanosomiasis americana* (Chagas' disease)—applies only in Lassance (Minas Geraes) and in no other Brazilian province or South American State.

KRAUS also attacks the question whether it is possible to distinguish clinically between endemic goitre and cretinism on the one hand, and the acute and chronic forms of Chagas' disease on the other. Generally speaking, the symptoms recorded by CHAGAS as characteristic of the acute stage of the disease, *e.g.*, fever, oedema, adenitis, enlargement of the liver and spleen, can be accepted as due to the trypanosomal infection ; but as regards certain isolated symptoms, such as goitre and myxoedema, one is bound to inquire whether these are not merely accidentally conditioned by the *genius loci*. CHAGAS himself believed that this was not the case, because many of his infected infants were fed exclusively on the breast and did not drink water ; KRAUS, however, points out that goitre and cretinism in the infant are often the result of goitre in the parents.

Very great difficulties are encountered in the clinical differentiation of the chronic form of Chagas' disease from endemic goitre and cretinism. In contrast to the acute cases trypanosomes are usually absent from the blood in chronic cases. KRAUS points out that the type and frequency of endemic goitre corresponds with the description of chronic cases given by CHAGAS. According to WAGNER-JAUREGG, in districts with endemic goitre and cretinism no hypertrophy of the thyroid is observed in 10 per cent. of cases ; all stages from normal thyroids up to voluminous goitre are encountered. As regards intelligence, all types are met with from intact to cretinoid, half cretin and absolute cretin ; and the cretins exhibit all phases from tottering gait to complete paralysis of the legs. In localities where cretins commonly occur cretinism is as frequent as imbecility. Apart from paralysis, which occurs in both diseases, athetosis, strabismus, aphasia, chorea and epilepsy are observed. As regards clinical myxoedema, it is believed by many that cretinism and myxoedema are identical ; the skin of the cretin shows the same trophic lesions and the same structure as in myxoedema. KRAUS accordingly reaches the conclusion that the clinical differentiation of the chronic form of Chagas' disease and endemic goitre and cretinism is a matter of the greatest difficulty.

KRAUS and his co-workers hence concluded that such conditions as goitre, cretinism, idiocy, aphasia, paralyses and infantilism are not the result of infection with *T. cruzi*, but are manifestations of an entirely independent condition, *viz.*, endemic goitre and cretinism. The main facts on which KRAUS and his colleagues base their contention can be summarized as follows :—

1. That CHAGAS's work was done in a hilly region of Brazil (Minas Geraes) where 75 per cent. of the native inhabitants have goitre and where a cretin, dwarf or paralytic occurs in every family. No cases of the disease have been recorded from the Brazilian plains, where infected bugs are also found.

2. That infected bugs have been found in almost every province in the northern portion of the Argentine. Whilst in many of these provinces goitre and cretinism are common, in certain of them (Córdoba, La Pampa and Buenos Aires) goitre and cretinism do not occur. Similarly, in Salta province where infected bugs and goitre and cretinism are common there exists one valley (Valle Calchacie) where, although infected bugs overrun the houses, goitre and cretinism are unknown.

3. Notwithstanding the wide distribution in the Argentine of infected bugs and of goitre and cretinism, KRAUS and his colleagues

had been unable to discover a single human being infected with trypanosomes.

4. It is impossible to distinguish clinically between the so-called chronic forms of Chagas' disease (the cardiac variety excepted) and endemic goitre and cretinism of Europe.

This can be said to summarize the position of knowledge of this difficult problem in 1926, when KRAUS wrote his final paper. During the last ten years, however, many new observations have been made which bear on the question of the relationship of Chagas' disease with endemic goitre and cretinism. As will be seen from the Table, no less than 83 human beings have now been discovered in the Argentine to be infected with *T. cruzi* ; these cases were distributed throughout all the provinces in the northern portion of the country, except Los Andes and Misiones.

These facts seem to warrant the general conclusion that in the Argentine cases of human infection will be found in all districts infested with bugs, provided they are searched for carefully. It is important, however, to observe that 5 of the 83 Argentine cases were discovered in Córdoba, where Kraus asserts that endemic goitre and cretinism do not occur, and that MAZZA and RUCHELLI (1934) discovered 2 acute cases of the disease in Tinogasta (Catamarca), where, they state, endemic goitre does not exist. . MAZZA and GUERRINI (1934) found 2 cases of the acute form of Chagas' disease at Anatuya in Santiago del Estero ; they add that they examined 101 children from this place without discovering any signs of goitre. Furthermore, careful study of the clinical protocols of the acute cases found in the Argentine reveals the interesting fact that many of them exhibited no enlargement of the thyroid ; this is in striking contrast with the observations of CHAGAS in Minas Geraes. It appears, therefore, that the distribution of human infection with *T. cruzi* in the Argentine does not coincide exactly with that of goitre and cretinism, the former infection being found in certain places where the latter condition does not exist ; and furthermore that many of the individuals in whom trypanosomes have been found exhibited no signs of thyroid enlargement or of hypothyroidism.

REICHENOW (1934), who has recently made a very careful study of the subject in Guatemala, found trypanosomes in only 3 cases, after repeated examination of the blood of about 100 children under 3 years of age living at Las Vinas. These children showed no sign of the disease, apart from possibly a little fever and slight oedema of the face and adenitis. REICHENOW stresses the fact that goitre and cretinism do not occur in Las Vinas and the surrounding districts.

The observations of MILLER (1931), of CLARK and DUNN (1932), of DECOURSEY (1935), and of JOHNSON and DE RIVAS (1936) in Panama are of special interest. Since the discovery of Chagas' disease in Panama in December 1930, 19 cases have been reported. Seven of the cases were in children under 3 years of age and three of them died. Of the non-fatal cases all but two were discovered as an incidental finding during malaria surveys of the Chagres River basin ; the symptoms and physical signs of Chagas' disease were practically absent, and such signs and symptoms as were discovered were mild and indefinite.

CLARK and DUNN emphasize the fact that 27 years of clinical and pathological records of the Panama Canal have shown no entry of a case of Chagas' disease, and that CLARK's experience in field surveys

for malaria in five mainland and three island countries of the Caribbean sea during a period of 3 years did not reveal a case, although over 65,000 men, women and children were examined. It seems, therefore, safe to assume that the group of conditions considered by CHAGAS to be characteristic of the chronic form of his disease must be extremely rare in Panama.

It is to be noted that of none of the Panama cases is it recorded that the thyroid was enlarged, or that there was any evidence of hypothyroidism. The post-mortem records of DECOURSEY's fatal case state that "the thyroid was firm, symmetric, and of normal size and color; it presented no microscopic lesion."

JOHNSON and DE RIVAS record that they inoculated a dog with the blood of one of their fatal cases. Trypanosomes appeared in the peripheral blood on the following day and were never absent from that time until the death of the animal 36 days later. The autopsy showed that the animal died from heart failure subsequent upon parasitic myocarditis; there was no enlargement of the thyroid. This observation is in harmony with what has recently been pointed out by ROMAÑA (1935), *viz.*, that, notwithstanding all the experimental research which has been caried out on this form of trypanosomiasis, no investigators have recorded any predilection on the part of the parasite for the thyroid gland, nor have they noticed hypertrophy of the gland as a result of their experiments.

The most recent work, therefore, must be held to have supported the contention of KRAUS (1926) that *Trypanosoma cruzi* was not responsible for many of the conditions, *e.g.*, goitre, cretinism, idiocy, aphasia, paralysis and infantilism, believed by CHAGAS to be chronic manifestations of the disease, and that the true interpretation of CHAGAS's observations is that his work was done in a region (Minas Geraes) where endemic goitre and cretinism are prevalent, and that in many of his cases the trypanosomal infection was superimposed on this disease.

Chronic cardiac form of Chagas' disease.—There still remains to be considered the question whether infection with *Trypanosoma cruzi* results in a chronic myocarditis. This problem is obviously one of the greatest importance, because of the large number of cases of chronic heart disease which have been recorded from various parts of South America. CHAGAS and VILLELA (1922) gave an account of no less than 62 cases which they designate as cardiac forms of American trypanosomiasis. The patients, who were between 11 and 54 years of age, exhibited such signs as tachycardia, bradycardia, alterations of conductivity, extra-systoles, auricular fibrillation, complete arrhythmia and alternating pulse. Each of the 62 cases is described in detail, and the paper is illustrated by numerous electrocardiograms.

GAMINARA (1923) writes that the cardiac form of Chagas' disease has been recorded in Uruguay, where infected bugs have been found, but no human being has as yet actually been proved to be infected with the trypanosome.

Scattered references to large numbers of people dying from syncope are found through the Argentine literature. ROMAÑA (1934*b*) described two cases, aged 40 and 51 years respectively, which he considered to be typical chronic cardiac cases of Chagas' disease in the northern portion of Santa Fé; trypanosomes were not found in the blood of these patients, but they gave a positive Machado reaction. In a footnote it is recorded that the first patient died suddenly (probably from syncope)

six months later. ROMAÑA draws particular attention to the large proportion of deaths from syncope in this district ; in Florencia, of 40 deaths 5 were from syncope, and in Guillermina 20 of 228 deaths were from syncope. In another paper ROMAÑA (1934*a*) described 2 acute cases of the disease from a place near the boundary of Santa Fé and Chaco. One of these children, who was kept under observation for 15 months, developed tachycardia and other signs of heart trouble; and ROMAÑA inquires whether " there is any relationship between this infection and the scarcity of old people which is so noticeable amongst our workers." Similarly MAZZA and GUERRINI (1934) state that in Añatuya (Santiago del Estero), where they found two acute cases of Chagas' disease, no less than 22 of a total of 233 deaths were due to syncope. JOHNSON and DE RIVAS (1936), in describing the post-mortem findings in one of their fatal cases of Chagas' disease, write : " On the basis of the gross findings at autopsy, the cause of death was given as secondary anaemia, due to intestinal parasitism with a resulting myocardial degeneration, and eventual heart failure. This is a rather common finding in small children in this locality." It was only when microscopic examination was made that the true cause of death was discovered to be an advanced degree of myocardial degeneration due to *T. cruzi.*

There is thus fairly clear evidence that myocardial degeneration and subsequent heart failure is a very common cause of death in many places in South America where infected bugs and cases of human infection with *T. cruzi* are known to occur. The evidence that the myocardial degeneration is to be associated with previous or actual infection with *T. cruzi* is, however, by no means so satisfactory. It has already been pointed out that the so-called chronic cardiac form of Chagas' disease has no counterpart in endemic goitre and cretinism of Europe. Furthermore, it is well known that both in acute cases in children and also in experimentally infected animals the parasite displays a pronounced predilection for heart muscle ; and there seems no reason to doubt that the chief cause of death in both these cases (children and animals) is parasitic myocarditis. We have to ask ourselves what happens in the majority of cases of Chagas' disease in which the heart lesions are not sufficiently severe to result in death during the acute stage of the disease. Unfortunately, very little is known. Attention has already been drawn to the observations of MAZZA and ROMAÑA (1934) and of these authors and PARMA (1935) on the changes found in the heart in two children who had died respectively from bronchopneumonia and from convulsions about a month after the commencement of the acute stage of the disease. In each case the interstitial tissue showed an intense infiltration by monocytes separating the muscle fibres from one another, and there was also evidence of a hyperplasia of connective tissue and a commencing fibrosis. These cases suggest that if the heart lesions are not sufficiently severe to kill the child in the acute stage of the disease the interstitial infiltration eventually undergoes fibrotic changes. It is, of course, quite conceivable that even though the infection itself dies out the fibrotic changes may seriously damage the heart, and, if certain parts of the heart are involved (*e.g.* Bundle of His), may give rise to the various manifestations described by CHAGAS, and finally to sudden death from syncope. As can well be imagined, it is exceedingly difficult to produce convincing evidence on this matter. We are informed by CHAGAS and VILLELA (1922) that of the 62 cases of the so-called chronic cardiac form of the

disease studied by them 5 died, and at post-mortem CROWELL discovered characteristic lesions with, in one case, numerous parasites. But it is not stated what these characteristic lesions were. TORRES (1928) gives details of the pathological lesions found at the autopsy of two persons aged 25 and 35 respectively, who died in Brazil in a region where trypanosomiasis is endemic, from what was considered to be the cardiac form of the disease. Both cases presented a parietal endocarditis, but in each the primary and essential lesion was a marked diffuse chronic myocarditis with the histological characters usually observed in Chagas' disease.

Whether these cardiac lesions are really characteristic of chronic Chagas' disease and can be distinguished from other forms of myocarditis, such as that due to syphilis, is open to doubt. The report of the Commission appointed by the National Academy of Medicine of Brazil (1924) records that in one case of the cardiac form of the disease, in whose blood the trypanosome had been found during life, the condition of myocarditis found at the autopsy was indistinguishable from a syphilitic process, although the Commission acknowledged that in Chagas' disease the Wassermann reaction is negative and antisyphilitic treatment unavailing.

A good deal of information regarding the Wassermann reaction in cases diagnosed clinically as chronic Chagas' disease is given by VILLELA and BICALHO (1923). Of the 33 cases examined only 9 gave a positive Wassermann reaction ; these included 17 chronic cardiac cases, five of which gave a positive Wassermann reaction.

It is interesting to note that VILLELA and BICALHO performed the Machado test on the same 33 cases. This test is a complement fixation test in which the heart and spleen of a highly infected puppy is used as antigen (*vide* later) ; all the cases except two gave a positive reaction. If the test has the significance which is attached to it by VILLELA and BICALHO, the results imply that 31 of these cases—cardiac, nervous, and hypothyroidic alike—were or had been infected with *T. cruzi.* It should be mentioned that VILLELA and BICALHO actually succeeded in demonstrating the presence of trypanosomes in 5 of 19 of these cases by inoculation of 10 cc. or more of their blood into guineapigs ; 2 of the positive cases were classed as chronic cardiac forms of the disease and 3 belonged to the goitrous and nervous forms. DIAS (1934*a*) records that the blood of 6 cases in the Oswaldo Cruz hospital, diagnosed clinically as chronic cardiac forms of Chagas' disease, gave a positive Machado reaction ; the blood of these patients was inoculated into guineapigs with 3 positive results.

The present position of the important problem of the relationship of the trypanosomal infection to the chronic myocardial disease can then be summarized briefly as follows :—

1. Cases of chronic heart disease characterized by tachycardia or bradycardia, alteration of conductivity, extra-systoles, auricular fibrillation, arrhythmia and syncope, are exceedingly common in many parts of South America, where infected bugs and cases of human infection with *T. cruzi* are known to occur ; and in certain districts syncope is responsible for a large percentage of the total deaths.

2. The parasite is known to have a predilection for the heart muscle, and the commonest cause of death in the acute cases is parasitic myocarditis.

3. The pathological changes observed in the hearts of patients who have died from the so-called chronic cardiac form of the disease are said by CHAGAS, CROWELL, TORRES and others to be characteristic. They apparently consist of an interstitial infiltration and fibrosis of the myocardium ; occasionally parasites have actually been found in these lesions in chronic cardiac cases.

4. In a number of such cases trypanosomes have been found in the peripheral blood, and a large proportion apparently give a positive Machado reaction. This, however, does not necessarily mean that the trypanosome infection is the cause of the heart condition, any more than the finding of trypanosomes in cases of goitre and cretinism implies that they cause this condition.

5. But if these cardiac lesions, so common in endemic regions, are not the result of the trypanosomal infection, it is not easy to assign a cause for them. They are apparently not found in endemic goitre and cretinism of Europe. Attention might be drawn to the syndrome described by ZONDEK as "myxoedema heart," the main features of which are general enlargement of the heart, an indolent heart action with slow pulse, and low or absent P and T waves in the electrocardiogram ; these cases are curable by thyroid and unaffected by digitalis. It is possible that some of the cardiac cases ascribed to Chagas' disease may have been confounded with this condition, but the frequency and severity of the cardiac lesions in regions where Chagas' disease is endemic, and its occurrence in some places where endemic goitre is absent, suggest that the so-called chronic cardiac form of Chagas' disease can hardly be identical with myxoedema heart. Possibly the condition may in part be due to syphilis, or the result of a secondary anaemia due to intestinal parasitism. Against the former hypothesis are the facts that the Wassermann reaction is usually negative and antisyphilitic treatment is said to be useless ; against the latter is the apparent absence of a similar state of affairs in other parts of the world, where intestinal parasitism is equally common.

There seems, on the whole, to be a *prima facie* case that American trypanosomiasis may actually be responsible for a good deal of the heart disease which is apparently so common in certain endemic areas in Brazil, Uruguay and the Argentine, and the cause of so many early deaths. The chronic cardiac form of the disease may be a sequel to an acute infection in infancy or the consequence of repeated infection in later life. If this should eventually prove to be the case, then American trypanosomiasis will indeed assume a pathological significance of the first magnitude. The subject is obviously one which urgently requires much further work. To reach a final conclusion will be a matter of no small difficulty, and probably the most fruitful line of investigation will prove to be the careful observation of cases of the acute infections in childhood, with adequate post-mortem examination of the fatal cases, and prolonged observation extending over many years of those which survive the acute attack, with the object of ascertaining whether they subsequently develop the characteristic cardiac manifestations. Such subsequent observation will necessarily involve repeated examination for the trypanosomal infection, the response to the Machado reaction (should this prove to be of real value as a test for the infection), and the elimination of syphilis and other infections and infestations which might conceivably give rise to chronic myocardial changes.

Diagnosis.

The diagnosis of American trypanosomiasis depends, of course, upon the discovery of the trypanosome, or upon obtaining satisfactory proof of its presence. Whilst this presents no great difficulty in the early acute stage of the disease, when the trypanosomes are to be found in the peripheral blood, the problem is very different in the later stages, when the trypanosome is confined to the heart muscle and other tissues, and only rarely appears in the blood, and then only in scanty numbers.

In the early acute stage of the disease, when the trypanosomes are usually present in fair numbers in the peripheral blood, the simple examination of fresh coverslip preparations of the blood, or of stained films, generally suffices to disclose their presence. When the parasites are too scanty to be detected in this way, inoculation of the blood into susceptible animals has been found to be of great value. The procedure most generally recommended is the inoculation of relatively large volumes (5 cc. to 10 cc.) of blood into guineapigs or puppies. By this method numerous observers—Bayma (1914), Carini and Maciel (1914), Tejera (1919), Niño (1928), Villela and Bicalho (1923), Torres (1930), Dias (1934*a*), Mazza (1934), Romaña (1936) and others—have succeeded in demonstrating the presence of trypanosomes in the blood when they were too scanty to be recognized by direct examination.

Another method of demonstrating the presence of trypanosomes in the peripheral blood when they are too few to be detected by the usual methods is that to which Brumpt (1914) gave the name "Xenodiagnosis." This consists in allowing the clean arthropod transmitter to feed upon the suspected carrier, and in ascertaining whether the bugs become infected. Care must be exercised in the application of this test, as it has been established that bugs can infect one another by coprophagy. The method has been used with success by Torres (1915), Torrealba (1934), Dias (1934*b*, 1935 and 1936*a*), Romaña (1936) and others. Dias records that he examined the blood (fresh and stained preparations) of 113 inhabitants of Lassance, Minas Geraes, with uniformly negative results. From 16 of these, blood cultures were made, and here again the results were negative. The xenodiagnosis test in 38 of the cases gave two positive results. Summarizing his work on this subject in his most recent paper, Dias (1936*a*) states that in all he has applied the test in 43 cases with 3 positive results; in his opinion it is a diagnostic method of great value.

In view of the ubiquity of infected bugs in many parts of South and Central America, it is a striking fact that trypanosomes have actually been found in so few human beings (excluding Minas Geraes, in only 117 cases). This is the more surprising as the parasite has evidently been carefully sought in many places where the disease is known to be endemic. Mazza (1926) found *T. cruzi* in the blood of one of 507 inhabitants of Jujuy, whom he examined for malaria; Geoghegan (1928) examined the blood of 1,600 people in Catamarca and found trypanosomes in two cases; Reichenow (1934) examined the blood of 103 children on three occasions in Las Viñas, Guatemala, and found 3 of them to be infected; and, notwithstanding the many thousands of blood films which have been examined in Panama, the trypanosome has so far been found in only 19 cases.

There are, however, certain considerations which make one hesitate to conclude that the infection is so rare as these records might suggest.

Attention has already been drawn to the fact that except in very young children the initial stage of the disease is usually so mild as rarely to require the attention of a physician. Such cases have accordingly been discovered only accidentally during systematic examination of the population for malaria, or because they exhibited some such sign as facial oedema, which caused the physician to consider the possibility of Chagas' disease, or, finally, because the infection happened to be superimposed on endemic goitre, which CHAGAS taught was one of the early signs of the disease. Again, it must be remembered that the period when the parasites are at all numerous in the peripheral blood is very limited—probably on the average not more than a couple of weeks or so. Whilst there is a considerable mass of evidence showing that with the subsidence of the initial febrile disturbance the trypanosomes either entirely disappear from the blood, or at least become so reduced in number that they can be found only occasionally, there is very little information regarding the length of time the infection actually survives in the human host. ZUCCARINI and OYARZABAL (1933) give details of a case which exhibited no signs of disease, except a micropolyadenitis, and in the blood of which trypanosomes persisted from May until September. ROMAÑA (1934*a*), in a region near the boundary of Santa Fé and Chaco, saw a child which was stated to have been bitten on the eyelid by a bug 8 days previously; there was oedema of the face, adenitis, and enlargement of the liver and spleen; the temperature was normal and the thyroid gland was not enlarged. ROMAÑA kept this child under careful observation for a period of 15 months. At the end of this period there was tachycardia, and the blood was infective for laboratory animals. MAZZA and BELMONT SÁNCHEZ (1936) give information regarding a boy aged 6 years who contracted the disease in July 1935, and was kept under observation until December 1935; during this period the blood was examined on 7 occasions and parasites were discovered on 5 of these, the last positive finding being on the 3rd December. A number of similar observations prolonged over periods up to 6 months are scattered throughout the Argentine literature.

REICHENOW (1934) supplies information bearing on the subject in respect of each of the 3 cases found by him in Guatemala. In the first case, a child aged 14 months with mild symptoms, trypanosomes were discovered in the blood on the 11th July, 1932; they were present for 18 days, and then disappeared and remained absent until 3rd December, when the observation ceased. In the second case, a child aged 17 months with very mild symptoms, trypanosomes were discovered in the blood on the 30th July, 1932 (a previous examination on the 16th June had been negative); trypanosomes were seen in the blood until August 6th, and were not found again until December 3rd, when, presumably, the observation ceased. In the third case, a child aged 14 months with very mild symptoms, trypanosomes were first discovered on the 7th November, 1932 (previous examination on the 7th and the 8th June and on the 28th July were negative); the blood remained positive until November 18th, after which it was negative until the observation ceased on December 3rd. REICHENOW describes how in each case the trypanosomes in the blood gradually became fewer and fewer until they finally could no longer be found either by direct examination or by subinoculation into guineapigs.

SEGOVIA (1922) records of the first case found by him in Salvador (1914) that it was well nine years after the infection was discovered;

he does not, however, furnish any information whether the patient was still infected. DIAS (1934*b*) records that he found trypanosomes in the blood of a goitrous idiot who had been twelve years in the Oswaldo Cruz hospital at Rio, where there was no possibility of contracting the infection ; he concludes, therefore, that the infection must in this case have persisted for at least twelve years.

On the whole it can be said that study of the literature indicates clearly that the patients have not been carefully observed for any length of time. Many of them have been watched for a month or two, and then, when trypanosomes had disappeared from the blood and the symptoms had subsided, they were lost sight of. Little attempt has been made to ascertain whether acute cases passed gradually into one of the chronic forms described by Chagas ; and we have no knowledge whether the disappearance of parasites from the blood is merely a temporary phenomenon or whether it is permanent, and whether their disappearance signifies that the patient is actually cured or merely that the parasite is localized in the heart or some other internal organ.

Parasites have, as has already been mentioned, been found in small numbers in the blood of a considerable number of chronic cases, but we have no means of deciding whether these patients have harboured the parasites in the heart or elsewhere for prolonged periods, or whether they were merely instances of recent re-infections. We know nothing about immunity in this infection, and it is possible that the chronic myocarditis, which is common in many endemic areas, may be the result of a summation of re-infections.

Machado reaction.—VILLELA and BICALHO (1923) attach very great importance to the value of the Machado reaction (GUERREIRO and MACHADO, 1913) as a diagnostic test in the chronic forms of Chagas' disease. They state that a glycerine and water extract of the heart and spleen of infected animals (puppies) is strictly specific ; the value of the antigen is directly proportional to the degree of parasitic infestation of the organs from which it was made. Extracts of the same organs from normal animals do not contain a complement-fixing antigen. There is no correlation between the Wassermann reaction and the Machado reaction, and the results are found to be entirely independent. VILLELA and BICALHO discuss the tests performed with the sera of 67 acute and so-called chronic forms of Chagas' disease, and were greatly impressed with the small number of negative results. These 67 cases comprise 19 tested by DA CUNHA and VILLELA, of which 14 gave positive results, 2 (acute cases) inconstant results, and 3 (1 nervous, 2 goitrous cases) negative results ; 15 tested by LEÃO, with 13 positive results and 2 (goitrous cases) negative results ; and 33 tested by VILLELA and BICALHO, 30 of whom gave positive results and 3 (2 cardiac and 1 goitrous) gave negative results. As is clearly shown there was no relationship between the Wassermann reaction and that of Machado ; in only 8 of the 33 cases examined by VILLELA and BICALHO was the Wassermann reaction positive. It is to be noted that trypanosomes were found in the blood of 5 of the 30 cases which gave a positive Machado reaction. Uniformly negative results were obtained when the Machado test was applied to normal persons or to persons suffering from other diseases.

LACORTE (1927) applied the test to 200 suspected cases of Chagas' disease in the hospital of Lassance (Minas Geraes) ; in 159 (79·5 per cent.) the reaction was positive. Of the 39 cardiac cases 87·2 per cent. were positive ; of 119 thyroid cases 79·5 per cent. were positive ;

of 6 nervous cases 100 per cent. were positive ; of 8 glandular cases 75 per cent. were positive ; and of 8 undetermined cases 25 per cent. were positive. In each of the 200 cases the Wassermann reaction was also performed, but in only 17 per cent. was it positive ; 13 per cent. gave both a positive Machado and a positive Wassermann reaction. Most of the patients with a positive Wassermann exhibited obvious syphilitic lesions. The test was also performed on 16 normal people and on 5 patients suffering from other diseases, with uniformly negative results.

VILLELA (1930) performed the Machado test with the serum of 186 patients coming from various places in Minas Geraes, and obtained positive results in 53 (29 per cent.). In 83 of these 186 cases the Wassermann reaction was also performed, with 17 positive results. As the following figures show there was no parallelism between the two reactions : Wassermann+Machado+in 2 cases, Wassermann+Machado—in 15 cases, Wassermann—Machado+in 23 cases. The 186 cases were all goitrous and were selected on this account The. positive cases were re-examined more carefully, and the great majority were found to exhibit cardiac disturbances, which could be recognized clinically or by electrocardiograms. VILLELA remarks that 90 per cent. of the chronic cardiac forms of Chagas' disease give a positive Machado reaction.

Other references to the value of the Machado test as an aid to the diagnosis of chronic Chagas' disease, and especially to the chronic cardiac forms, are scattered throughout the literature.

DIAS (1934*a*) inoculated guineapigs with the blood of 6 cases of the chronic cardiac type, giving a positive Machado reaction, with 3 positive results.

MAZZA (1934) in Jujuy State of the Argentine found that 1 of 20 goitrous idiots gave a positive Machado reaction, and that inoculation of the blood into a guineapig produced infection. A second goitrous idiot was found to give a positive Machado reaction in the same district, but animal inoculations were negative. MAZZA and CORNEJO (1934) examined a number of cretins and idiots in Salta province and found 3 who gave a positive Machado reaction ; attempts to demonstrate infection by animal inoculations of the blood and by biopsies of the deltoid muscles failed.

EV. CHAGAS (1934*a*, *b*, *c*) gives very interesting information regarding the Machado reaction in a case of malignant disease which he infected experimentally with *T. cruzi*. Before infection the Machado reaction was negative, but as early as 10 days after inoculation the patient's serum gave a positive reaction ; the reaction was more intense on the 17th day and strongly positive on the 26th day. This patient lived for 6 months after the experimental infection, and during the whole of the time the Machado reaction remained strongly positive. EV. CHAGAS, in commenting on this fact, remarks that it is known that individuals who have been removed from an endemic area, and who have not been exposed to re-infection, may continue to give a positive Machado reaction for at least 15 years. The case referred to above by DIAS (1934*b*) presumably falls into this category. The patient, a goitrous idiot of 32 years of age, coming from Lassance, Minas Geraes, was admitted to the Oswaldo Cruz hospital in 1922. In 1934, after she had been 12 years in hospital where she was not exposed to re-infection, the serum gave a positive Machado reaction, and the presence of *T. cruzi* in the blood was proved by inoculation into a guineapig and by the method of xenodiagnosis.

In a recent paper KELSER (1936) has described a modification of the complement fixation test. He points out that in all previous work the antigens employed had been prepared from organs of laboratory animals artificially infected with *T. cruzi*; and that the extent of infection of these organs and the potency of the antigens made from them differed markedly. In order to resolve this difficulty, KELSER devised a method of preparing antigen from artificial cultures of *T. cruzi*. He states that with the aid of this antigen he has tested over 400 serum specimens, including a number of known cases of Chagas' disease, in man and lower animals. The test proved positive in all known cases of the disease from which sera were available, and negative where there was no evidence of Chagas' disease. Tests of numerous Wassermann-positive sera indicated that no difficulty will be experienced from cross reactions in connexion with the two diseases.

Whilst the evidence is probably as yet insufficient to warrant a definite opinion regarding the significance of the Machado reaction, sufficient work seems to have been done to indicate that it cannot be brushed aside as unworthy of serious investigation. It is clear that a positive reaction is given by large numbers of people in the endemic areas, and that quite a number of the positive cases have been proved to be infected with *T. cruzi*. It also seems evident that there is no parallelism between the Machado reaction and the Wassermann reaction.

The diagnosis of Chagas' disease in the absence of trypanosomes in the peripheral blood is a matter of great importance, and the more so since trypanosomes occur in the blood for so short a period and in such scanty numbers. It is conceivable that the Machado reaction may prove specific, and in this case it will assume that same importance in Chagas' disease that the Wassermann reaction has in syphilis. In how many cases of the latter disease does the diagnosis depend upon the discovery of the parasite? If we exclude the primary cases, we have to admit that almost invariably we rely upon the Wassermann reaction; and Chagas' disease resembles syphilis in that it is extremely difficult to find the parasite, except in the early stage of the infection.

The matter is obviously one which urgently demands thorough investigation. It must be ascertained whether the Machado reaction is given by persons living in non-endemic regions, or whether it is only given by persons living in endemic districts. A simple observation of this sort would undoubtedly help to clear up the problem. If it should prove to be the case that positive reactions are only obtained in endemic areas, the case for associating it with Chagas' disease would be greatly strengthened. We should then have to proceed to the investigation of what would probably prove to be the much more difficult problem of ascertaining whether a positive reaction implied actual infection or merely that the patient had once been infected with the disease.

There is a considerable mass of data which indicates that possibly American trypanosomiasis is responsible for an enormous amount of human disease in the huge endemic areas of South America, and any test, such as the Machado reaction, which may throw light on the matter, is well worthy of the most careful investigation.

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LEPROSY.

LEPROSY REVIEW. 1936. Oct. Vol. 7. No. 4. pp. 151–200. With 32 figs. & 3 maps (1 double) on 7 plates. Quarterly Publication of the British Empire Leprosy Relief Association, 131 Baker Street, London, W.1. [2*s*.]

In this issue Dr. E. Muir records the impressions he formed during an extensive tour in West Africa, visiting the centres of leprosy work. The first article is a report on leprosy work in Nigeria with suggestions for improving it by adopting a policy which in time will enable the disease gradually to be brought under control, and eventually, eliminated. A table of the present leper institutions shows fourteen government Leper Settlements or Colonies with 2,229 inmates, and seven medical mission institutions for 2,793 patients, together 5,022 out of an estimated total of 200,000 lepers in Nigeria, or 1 to every 35 to 40 cases. Several of the smaller institutions are only homes for incurable cases of a charitable nature. There are, however, five large settlements under whole-time officers with an atmosphere of activity and hopefulness, the largest being at Itu with 1,500 cases, but the expense of increasing these to control effectively the spread of the infection would be prohibitive.

Muir therefore suggests the organization of the work on a provincial basis under Leprosy Boards, to meet annually at the provincial settlement and be responsible for the initiation, development and co-ordination of all anti-leprosy efforts in the province. With the provincial settlement as the centre for examining, treating patients, training anti-leprosy workers, clan settlements of an inexpensive nature would be organized to provide for the majority of the lepers of each clan after surveys. Provision should be made as far as possible in each of these for separation of infants from infectious parents. The main settlements can be most efficiently and economically administered under mission doctors, and the Native administrations in each province should be jointly responsible for the upkeep of their provincial settlement. Lay workers and nursing sisters should be able to supplement the work of the medical staff. Each settlement should have four or five hundred acres of land within easy reach of a good road and will provide work for the lepers. Good buildings should be provided for the staff, and cheap huts can be erected at little cost by the patients for their own accommodation. Infant welfare will be an important feature. A leprosy expert should be provided for Nigeria to spend some time in each of the provincial settlements in turn.

A Forest Plantation already possesses 4,640 *Hydnocarpus wightiana* trees for the supply of the pure oil for injections at much less cost than the esters, and further seedlings are available for planting out. A further article gives details of local interest of the Nigerian Leper institutions.

Leprosy in the Gold Coast is the subject of another article on similar lines, and the needs of the smaller colony of Sierra Leone are also dealt with. *L. Rogers.*

BROWN (James A. K.). **Leprosy in Southern Nigeria. Problems of Treatment and Control.**—*West African Med. Jl.* 1936. Oct. Vol. 9. No. 1. pp. 10–14.

This article deals with the leper settlement at Uzuakoli with 1,082 inmates in 1935—an increase due to the admission of patients prepared

to maintain themselves, in addition to those sent by the Native Administrations, but many still have to be refused admission for want of accommodation. Thirty were discharged during the year, and children born in the colony are from their birth brought up in a special ward. About 20 per cent. are early, 60 per cent. advanced but able-bodied, and 20 per cent. disabled patients. Farming on the more satisfactory individual system and constructing houses afford most of the work on the 340 acres of land. One doctor forms the European staff, but a native one is being trained. In addition to the treatment of complicating diseases injections of the crude oil and esters combined with cod liver oil are used, and the production of a mild reaction with a single rise of temperature to from 99·2° to 99·6°F. is aimed at. With attention to detail it has been found that the children can be brought up from birth on good artificial foods and properly balanced diet without difficulty. The disease is believed to be spreading, so such well administered colonies as this are urgently needed, as well as outlying dispensaries to meet the needs of further patients. *L. R.*

ADVIER (Marcel). La lèpre à Madagascar. [**Leprosy in Madagascar.**] —*Internat. Jl. Leprosy.* Manila. 1936. July–Sept. Vol. 4. No. 3. pp. 337–342. With 1 fig. (map).

The unsuccessful attempts to stamp out leprosy by compulsory isolation are narrated in this article. A law ordering isolation of all lepers has long been in force in Madagascar, and a number of leprosaria have been provided under missionaries. A new stringent law was promulgated in 1911 ordering isolation of all forms of the disease, and some 3,000 lepers are cared for in colonies and 300 in leper villages out of 6,000 believed to exist in the island. In 1915, 5,675 were enumerated, but are now believed to have been reduced to 3,000, chiefly through deaths during an influenza epidemic with 80,000 mortality in the island. Curative treatment is important, and has been too much neglected up to now. *L. R.*

DE MELLO (I. Froilano) & PEREIRA (O. Loyola). **Some Facts concerning Leprosy in Goa.**—Reprinted from *Indian Med. Jl.* Vol. 30. No. 7. 4 pp. With 1 chart.

Through the influence of Colonel de Mello, anti-leprosy work has been carried on in this French possession in India since 1925. Visits to the villages of known lepers revealed 240 active cases, and they are believed to total 300. A central colony was established in 1932 through which 179 lepers have passed and 140 are resident there, 67 only of whom are known to have had intimate contact with a leper. A few have been cleared of all symptoms and infectivity. *L. R.*

CEYLON. Sessional Paper XX.—1936. **Leprosy in Ceylon. Report of Second Visit of Investigation carried out from November 2 to December 5 by Invitation of Ceylon Government** [COCHRANE (Robert G.)]. 1936. Sept. 29 pp. Colombo: Govt. Press. [30 cents.]

This is a report on a second visit to Ceylon of a month's duration. Dr. Cochrane found considerable progress in the previous two and a-half years. The too rigid provisions of leprosy Ordinance have been suspended and a survey instituted. Compulsory measures are now

only used for isolating open infectious cases. Early neural cases in children should not be kept with open ones. An effective leprosy prevention centre has been organized in Colombo.

One object of his visit was to acquire further data on early infections in children, and by a re-examination of 61 under the age of 18 years approximately 67 per cent. were found to be improved or stationary without treatment, and nearly all who had become worse had a history of close contact with an infectious case, but he admits the numbers are small. Good follow-up work had been done in connexion with some of the clinics. Most of the report is taken up with details of local conditions and suggestions for improvements. *L. R.*

MILLS (Clarence A.). **World Leprosy in Relation to Climatic Stimulation and Bodily Vigor.**—*Internat. Jl. Leprosy.* Manila. 1936. July–Sept. Vol. 4. No. 3. pp. 295–314. With 2 figs. [28 refs.]

This article attempts to explain the distribution of leprosy in relation to the effects of climate on bodily vigour. The author states that cool, changeable weather leads to high energy levels and active life, while prolonged moist heat has the opposite effect. He concludes that areas with a stimulation index below 3·0 are cursed with leprosy, with an index above 6·0 the disease becomes mild and less prevalent and above 12·0 the disease is only continued by the importation of cases. To explain the obvious exceptions he states that: "The last wave of leprosy in Norway coincided to a remarkable degree with a world-wide period of subnormal temperatures and increased storminess. On the other hand, when the disease spread with such virulence over Europe in the Middle Ages, the earth was under the influence of a major heat wave that sapped the vigor and vitality of population masses in temperate zones." He therefore advocates the Utopian measures of the segregation of lepers in the most stimulating regions available and the removal of the children of lepers to the same areas, as well as "the use of artificial climatic stimulation by indoor air-conditioning methods." *L. R.*

ALEIXO (A.). Investigação, epidemiologia, estatistica de lepra—da sua importancia na prophylaxia da endemia leprosa.—*Brasil-Medico.* 1936. May 2. Vol. 50. No. 18. pp. 377–379.

TESCH (J. W.). Iets over lepra in Midden-Celebes en de leprozenkampong bij Paloe.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1936. Nov. 3. Vol. 76. No. 44. pp. 2829–2840.

TRUONG-VAN-QUE. De la lutte antilépreuse en Indochine. [**Leprosy Control in Indo-China.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1936. May. Vol. 14. No. 5. pp. 408–411.

In this brief paper the author first quotes the suggestion of MONTEL to adopt milder measures against leprosy than compulsory segregation, including treatment in dermatological clinics, but thinks the Indo-China government will hesitate to free all lepers. He therefore suggests that uninfective cases should be set at liberty, and to distinguish these he considers that four injections of methylene blue should be given, and those whose lesions become coloured blue should be classed as dangerous.

L. R.

ANDERSON (Hamilton H.). **The Possibilities of Chemo-Prophylaxis in Leprosy.**—*Folha Med.* 1936. July 25. Vol. 17. No. 21. pp. 311–313. [20 refs.]

The author makes suggestions based on an hypothesis for the verification of which he has no clinical material. After references to some recent literature on the use of dyes in leprosy and the possibility of nasal infection, he suggests that dyes, possibly combined with chaulmoogra preparations, might be applied to the nasal area of newborn susceptible individuals in leprous households, and in another experimental group dilute solutions might be applied frequently to the skin during the first three years of life as a prophylactic measure.

L. R.

RODRIGUEZ (Jose). **Our Leprosy Problem in the Philippines.**—*Monthly Bull. Bureau of Health.* Manila. 1936. May. Vol. 16. No. 5. pp. 161–179. With 3 figs. [11 refs.]

The author considers whether the costly segregation system of the past 28 years might not be modified with advantage.

In a brief review of compulsory segregation measures in other countries he points out that little success has been obtained except in Norway. The well-known attempt to enforce segregation in the Philippines is then narrated, during which hiding lepers had " to be hunted like wild beasts. Not a few were shot down resisting arrest." In 1920 improved treatment enabled some cases to be paroled with good effect, and in 1928 treatment stations for hopeful positive cases increased voluntary admissions to such an extent that during the last five years 75 per cent. of admissions to them have been entirely voluntary. Skin dispensaries have also proved of value. " In other words, the Government is now trying to cure them at the earliest stage possible and before there is need of isolating them. The present policy is certainly more logical, more humanitarian, and much more economical than the former one."

The later part of the paper deals with the results of segregation, which is illustrated by a curve. This shows a fairly steady rise in the number of segregated lepers, which only include bacteriologically positive cases. The early rise was due to the gradual discovery of cases. The curve flattened out from 1923 to 1927, the subsequent rise being due to opening of local detention and treatment stations in addition to the great Culion settlement, with the attraction of earlier cases. Further, the new cases segregated year by year have been becoming earlier ones (although, unfortunately, the figures of the number found each year are not available), and that advantage is not brought out by the curve. The death rate has also much decreased, and this adds to the numbers remaining segregated. In the Cebu Province there has been a slight fall in the new cases. *L. R.*

DENNEY (O. E.). **The History of Leprosy in Louisiana.**—*Public Health Rep.* 1936. July 31. Vol. 51. No. 31. pp. 1029–1034.

This is a brief account of the well-known leprosy infection of this Southern United States province, partly by French families from Canada and partly by negro slaves from Africa. Whites still show the greater number of cases. The Carville settlement was founded in

1894, and became a federal institution in 1921, and still contains 94 Louisiana patients, no decrease having resulted from the compulsory segregation. *L. R.*

LUTZ (Adolpho). **Transmission of Leprosy and Prophylactic Indications.** —*Mem. Inst. Oswaldo Cruz.* 1936. Vol. 31. No. 2. pp. 383–390.

Writing with half a century of experience the author discusses transmission and prophylaxis. Although due to a germ he holds that it is not contagious, and he prefers to call the organism a Coccothrix rather than a Mycobacterium. He points to the failure of inoculation experiments as against direct contagion, and concludes that it must be transmitted by a living agent. He then discards all bloodsucking insects except the mosquito, such as fleas, lice, bugs and mites, on account of their ubiquitous occurrence, and concludes that the mosquito must be the carrier. This leads him to advocate mosquito protection as the one effective prophylactic measure against leprosy, and this should not be postponed " any longer, on the plea that experimental proof has not been given." *L. R.*

COCHRANE (Robert G.). **Prevention of Leprosy with Special Reference to Children.**—Reprinted from *Jl. Christian Med. Assoc. India, Burma & Ceylon.* 1936. July. 12 pp.

——. **Early Leprosy.**—*Ibid.* Sept. 4 pp.

——. **Leprosy in Children in Ceylon.**—*Leprosy in India.* 1936. Oct. Vol. 8. No. 4. pp. 147–150.

The author emphasizes the very generally acknowledged importance of protection of children from infection in attempts at prophylaxis. After mentioning the figures in his recent Ceylon report (1935) on the frequency of mild cases among children, he expresses the opinion that superinfection with the development of severe types may result from mild cases being exposed to further infection, and he is in agreement with MUIR and others regarding the importance of diet and good economic condition in increasing resistance to the disease. He thinks when the incidence is low in children in any place the problem is not serious there. He agrees in the importance of observation of contacts, and the isolation of infective cases, leper villages being advocated where settlements are not practicable.

In a further paper on early leprosy he also deals with mild cases in children, and gives a brief description of the early symptoms. *L. R.*

LOWE (J.). **A Study of Macules in Nerve Leprosy with Particular Reference to the " Tuberculoid " Macule.**—*Leprosy in India.* 1936. July. Vol. 8. No. 3. pp. 97–112. With 35 figs. on 7 plates.

The author discusses the high incidence in Calcutta of macular lesions with the occurrence of tuberculoid changes, and describes in detail the clinical, pathological and bacteriological features of the types of macule seen in nerve cases, with a number of good photos of the naked eye and two of the microscopical appearances. Acid-fast bacilli were found in practically all the active macules, and they had a marked tendency to heal spontaneously. He considers that the different types of macule seen in nerve leprosy are manifestations of a tuberculoid

type of inflammatory changes in different stages of activity and quiescence. Caseation may result from marked reaction of the tissues to the ordinary acid-fast organisms, and not to a special strain or filter passing form, or to trophic nerve disturbance. The more acute inflammatory changes in tuberculoid lesions have been attributed to lepra reaction, but they are followed by subsidence, and not by the increase of the leprous infection following reactions in nodules. In a classification the neural, or maculo-anaesthetic, lesion should be distinguished from the nodular or cutaneous type as the macular lesions have a very much better prognosis. *L. R.*

WADE (H. W.). **Regional Variations of Leprosy with Special Reference to Tuberculoid Leprosy in India.**—*Indian Med. Gaz.* 1936. Nov. Vol. 71. No. 11. pp. 653–659. [22 refs.]

This is an interesting contribution to variations in the incidence of the tuberculoid type of lesion in different countries and areas, partly based on a recent four months' investigation in India. The author points out that the great variations in the types of leprosy in different countries may lead to descriptions of the disease based on experience in one area being far from correct as applied to another region. This is brought out by variations in the proportion and severity of the nerve and cutaneous forms ; for in India, and especially in Calcutta, the mild neuro-macular or tuberculoid type is unusually common, and the severe nodular cutaneous comparatively rare, especially in comparison with the great incidence of the latter in Japan. The proportion of serious eye complications illustrates this point, for the proportion varies from 1 per cent. in Culion and the Federated Malay States, through 2·9 per cent. at Purulia in India, to 8·6 per cent. in the U.S.A. Carville colony, and 18·2 per cent. at Zensei in Japan. Alopecia is also common only in Japan and South Africa, and cold abscesses in the nerve trunks only in India. In conclusion he pays a tribute to the work of the Calcutta Research Centre at the School of Tropical Medicine. *L. R.*

JUNIOR (Rabello). Novas provas contrarias á inclusão da variedade tuberculoide da lepra na forma nervosa. [**Tuberculoid Leprosy : Reasons for not regarding it as of the Nervous Form.**]—*Brasil-Medico.* 1936. May 9. Vol. 50. No. 19. pp. 397–398.

This article is a discussion of the question of the classification of tuberculoid leprosy. Laboratory returns show that the serum reaction of Witebsky, Klingenstein and Kuhn is positive in about 90 per cent. of lepers suffering from the cutaneous form and about 70 per cent. with the nervous form, whereas in tuberculoid leprosy the proportion of positives is less than half. We must distinguish, says the author, miliary ulcerous tuberculosis and cutaneous leprosy with visible bacteria on the one side, and tuberculides and tuberculoid leprosy, with sarcoid and tuberculoid forms, but without recognizable bacilli on the other. Tuberculoid leprosy in his view is a " variant " in the evolution of normal leprosy, neither cutaneous nor nervous. He presents a scheme of classification in which he places it under the group of the early or transitional phase of the cutaneous form, with focal inflammation, bacilli scarce or absent, and subdivides it into (1) cuticular nodules ; (2) subcuticular nodules ; (2) serpigenous ; (4) erythematous ; and (5) follicular or lichenoid. When the leprosy is in a later stage, with bacilli abundant, he calls the lesions lepromata and distinguishes

five types: erythematous, tuberous, nodular, papular and infiltrative. [Whether such distinctions can be clearly made out between lepromata and tuberculoid leprosy, and the various subdivisions of each, can only be determined by those with long experience.] *H. H. S.*

HUIZENGA (Lee S.). **Development of Leprosy Clinics in the Control of Leprosy.**—*Amer. Jl. Public Health.* 1936. Sept. Vol. 26. No. 9. pp. 883–887.

After a reference to such old leprosy clinics as that at the hot sulphur springs about Kasatsu in Japan and some in China, the author points out that a chain of "leprosy clinics now girdles the world" and is replacing forced segregation, and he advocates the organization in all leprous areas of large central clinics, with surrounding small out-lying ones to reach as many cases as possible, such as are now found in India, the Philippines and the Dutch West and East Indies. In China 80 per cent. of such clinics are carried on at special times in general hospitals, and 20 per cent. associated with leprosaria, the latter being the more efficient, and they are nearly all carried on by missionary bodies, but in view of China being the most heavily infected area in the world he concludes: "What are these among so many?" *L. R.*

LARA (C. B.). **The Problem of the Follow-up of "Negative" Lepers.**—*Monthly Bull. Bureau of Health.* Manila. 1936. Feb. Vol. 16. No. 2. pp. 39–47.

SAMSON (Jose G.). **On the Follow-up of the Released Negative Leper.**—*Ibid.* May. Vol. 16. No. 5. pp. 180–186.

These two papers give somewhat conflicting data. Lara, after pointing out that there is no provision for the systematic periodic examination of relatives and other contacts of known lepers, goes on to point out that the regulations for following up the discharged "negative" lepers, now amounting to approximately 3,500, and providing them with further treatment, are very inadequately carried out for want of sufficient staff and funds. He asserts that, judging from the findings of isolated surveys, probably 46 per cent. or more have already relapsed and may become a danger, although no evidence is adduced that any healthy persons have actually been infected by such.

Samson also admits the inefficiency of the present follow-up system, but states that in one examination of paroled negatives, 22 of 288 were found to have become bacteriologically positive, or only 8 per cent., but points out that repeated examinations at intervals would reveal a higher figure. Improvement in the follow-up system is advocated.

L. R.

PLANTILLA (Fidel C.). **Transmission of Leprosy. I. Sites of the Single Leprotic Lesions.**—*Monthly Bull. Bureau of Health.* Manila. 1936. Apr. Vol. 16. No. 4. pp. 137–141. With 3 figs.

This paper deals with the surface distribution of single, but established, leprotic lesions in 266 early cases seen at the Philippines Cebu skin dispensary. The most frequent locations were on the cheeks, elbows, extensor surfaces of the forearms, buttocks and knees, especially in children under 14 years, and they were fairly frequent on the arms, hands, fingers, legs and feet, but rare on the chest, abdomen, back and

thighs. He points out that the most infected areas are the exposed surfaces of the body most lain upon when being carried and when sitting and playing, and most subject to direct skin contact between the mother and child. These facts indicate direct infection from contact with the mothers or with the chair, floor, bedding or soil. *L. R.*

DOW (D. P.). **Late Results of Nerve Decapsulation in Leprosy.**—*Leprosy in India.* 1936. July. Vol. 8. No. 3. pp. 113–118.

The author records the later results in eighteen cases of nerve decapsulation, mainly for the relief of agonising pain by removal of the nerve sheath at the main seat of pressure. Unfortunately the periodic re-examination of such patients has not confirmed the sanguine hopes of this operation, for in no case has the improvement been maintained, and in some the condition had become worse than before the procedure. This is due mainly to fibrous tissue formation at the site of the operation and to pressure on other parts of the nerve by the disease process. An alternative and better treatment is intradermal injection of the Hydnocarpus esters along the course of the thickened nerves. In the case of abscess formation along a nerve the caseous material should be removed and the wound closed without drainage. *L. R.*

MUIR (Ernest). **Prognosis in Leprosy. I & II.**—*Lancet.* 1936. Aug. 15 & 22. pp. 391–392 ; 448–449.

The main points in this informative article based on an immense experience are the following :—The two main factors are the concentration and distribution of the lepra bacilli in the body and the resistance of the patient to the infective process. Localization of the disease to one or more nerves and the adjacent skin implies high resistance and a good prognosis as long as the general health of the patient is maintained, as there is a tendency to resolution. In more general infections of the skin and nasal mucous membrane, with abundant lepra bacilli and infiltration of the dermis, the prognosis is much more serious. General resistance is least in early childhood, when exposure to infection most commonly leads to serious disease, but the older the child on first exposure the more likely is the infection to prove mild. A high erythrocyte sedimentation reading and negative or weak leprolin tests indicate low resistance. Extensive distribution of nodular lesions containing many bacilli and the appearance of rapidly growing new lesions furnish a grave prognosis ; but few macules with thickening or tenderness of connected nerves and few bacilli in the macules are favourable points. Any debilitating complicating disease is a grave handicap. *L. R.*

LEFROU (G.) & DES ESSARTS (J. Quérangal). Contribution au diagnostic des faux lépreux. (Deuxième mémoire.) Les macules dyschromiques d'épidermomycose. [**Diagnosis from Skin Fungal Diseases.**]—*Bull. Soc. Path. Exot.* 1936. July 8. Vol. 29. No. 7. pp. 743–749.

The authors discuss the differentiation of leprotic lesions from those of *Microsporon furfur* and *Pityriasis versicolor*. For this purpose they rely mainly on the absence of loss of sensation in the later fungal infections of the skin and on finding their respective causative vegetable parasites by microscopical examination. *L. R.*

MARCHOUX (E.) & CHORINE (V.). La sensibilité au virus lépreux n'est pas plus grande chez les jeunes que chez les adultes. [**Susceptibility to Leprous Virus is no greater in the Young than in the Old.**]—*Ann. Inst. Pasteur.* 1936. Dec. Vol. 57. No. 6. pp. 583–596. With 3 figs.

This paper deals with the susceptibility to leprous infections based on experiments on rat leprosy. The frequent contamination of young children by their leprous parents is emphasized, and this is confirmed in the case of inoculated rat leprosy by the much greater extent of the lesions, and active infection by much smaller doses, of young than of old rats. Again, in the case of the rat disease hereditary infection is not proved, and they are not in agreement with the hypothesis of some American writers that a hypothetical virus stage of the lepra bacillus is the cause of infection and not the bacilli themselves. Adult rats may become infected by surprisingly brief contact with infected rats in the ulcerative stage. Experiments made in their laboratory prove the passage through porous bougies of typical bacilli of Stephansky, and the non-existence of an ultra microscopical virus. They also hold that the lepra bacilli frequently reported to have been found in the cords of newly-born infants are dead organisms. They conclude that the frequent infections of young children are due more to the facilities for their infection than simply to their greater susceptibility. *L. R.*

ITAKURA (Teiju). Zahnärztliche Untersuchungen bei Leprakranken. III. Bericht: Klinische Betrachtungen der leprosen Mundhöhlen-Veränderungen bei leprakranken Formosa-Chinesen (Fokien-Stamm).—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1936. Nov. Vol. 35. No. 11 (380). [In Japanese pp. 2474–2489. [27 refs.] German summary pp. 2489–2491.]

LIE (H. P.). **Tracheitis and Bronchitis Leprosa.**—*Internat. Jl. Leprosy.* Manila. 1936. July–Sept. Vol. 4. No. 3. pp. 281–288. With 8 figs. on 2 plates.

This is an illustrated account of the macroscopical and microscopical lesions found after death in the trachea and bronchi. In certain cases these may be extensive. Traumatism of various kinds may produce or predispose to such lesions. The leprosy bacilli may pass through the mucous membrane to invade the deeper tissue without producing any macroscopic lesions of the mucous membrane. *L. R.*

i. LAMPE (P. H. J.). Motiveering en uitvoering van een onderzoek naar omstandigheden en verhoudingen in leprarijke en lepra-arme gebieden. [**Investigation in Leper Countries.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1936. Aug. 25. Vol. 76. No. 34. pp. 2117–2123. English summary.

ii. DARWIS (A.). Het lepra-onderzoek in Lamongan. [**Study of Leprosy in Lamongan.**]—*Ibid.* pp. 2123–2128. English summary.

iii. SOETOMO (R.). Enkele stellingen over de lepra [**Some Points in Leprosy.**]—*Ibid.* pp. 2129–2132. English summary.

iv. THIERFELDER (M. U.). Enkele opmerkingen over het ontstaan der lepra. [**Remarks on the Aetiology of Leprosy.**]—*Ibid.* pp. 2133–2137. English summary.

v. FISCHER (J. A.). Tuberculinetherapie bij lepra. [**Treatment of Leprosy by Tuberculin.**]—*Ibid.* pp. 2138–2146. With 1 plate. English summary.

vi. LAMPE (P. H. J.) & DE MOOR (C. E.). Ratten-Lepra. Vierde mededeeling: Zuurvaste saprophyten; aanteekeningen bij het kweekonderzoek van rattenlepra. [**Attempts at Cultivation of the Organism of Rat Leprosy.**]—*Ibid.* pp. 2147–2153. With 2 figs. on 1 plate. English summary.

vii. MÜLLER (H.) & SOETEDJO MERTODIDJOJO. Doodsoorzaken en viscerale afwijkingen bij lepralijders in Oost-Java. [**Findings in Autopsies on Lepers in East Java.**]—*Ibid.* pp. 2174–2184. With 5 figs. on 1 plate. [18 refs.] English summary (8 lines).

The following are the main points of interest in this series of papers.

i. Dr. Lampe pleads for investigation of the reasons for the variable incidence of leprosy in different countries, and mentions the initiation of one.

ii. A. Darwis records the frequency of infections among brothers and sisters.

iii. R. Soetomo finds most infections originate in rural districts.

iv. M. U. Thierfelder assumes that infection is transmitted through an intermediate host, and suspects the body louse as the agent.

v. J. A. Fischer reports on the use of tuberculin combined with injections of leprolin with hopeful results.

vi. Lampe and de Moor record negative attempts to cultivate the rat leprosy bacillus, only saprophytic acid-fast bacilli growing.

vii. H. Müller and S. Mertodidjojo report on 225 autopsies and found tuberculosis and pneumonia the main causes of death and lesions in the testes and spleen to be common. *L. R.*

DES ESSARTS (J. Quérangal) & LEFROU (G.). Evolution des léprides en lépromes. [**Evolution of Leprides and Lepromes.**]—*Bull. Soc. Path. Exot.* 1936. Nov. 18. Vol. 29. No. 9. pp. 945–949.

The author states that DARIER contended that anaesthetic macules are of the same nature as nodules with every gradation between them, but the present writers makes the following distinctions:—Clinically the former show much less thickening of the skin. Histologically the nodules present a granulomatous appearance which is not so marked in the other type. Bacteriologically the organisms are very numerous in the nodules but scanty in the nerve macules. *L. R.*

CLOUSTON (Thomas M.). **An Investigation into the Thick Blood-Drop Method of Diagnosis in Leprosy.**—*Med. Jl. Australia.* 1936. Sept. 26. 23rd Year. Vol. 2. No. 13. pp. 430–432. [13 refs.]

Working in the Island of Nauru, where early diagnosis is of such great importance in the successful campaign against a serious epidemic of leprosy, the author describes a simple method of searching for lepra bacilli in blood obtained by puncturing the skin after rejecting the first drops. A thick drop of blood is dried in the air, dehaemoglobinized in distilled water, dried again and stained by the Ziehl-Neelsen method. Nodular cases were first investigated with positive results in 77·7 per cent. Thirty-six segregated cases with milder cutaneous lesions gave only two positive results. The results were negative in all of 21 early patients attending out-patients clinics, and also in ten suspects and eight

children of lepers. These results support those of Lowe in India. The method is thus of no practical use in the detection of early or latent leprosy. *L. R.*

ANDERSON (Hamilton H.), CERQUEIRA (Paulo), ANDERSON (Jeanette van D.) & PORTUGAL (H.). **Clinico-pathologic Studies of Leprosy in Brazil.**—*Amer. Jl. Trop. Med.* 1936. Nov. Vol. 16. No. 6. pp. 689–697. With 2 figs.

Leprosy in Brazil shows no preference as regards sex, but those of the white race are attacked twice as frequently as the coloured, and the majority are labourers, domestics or engaged in trade. The lower extremities are first involved, and after five years more than half the body may be affected, with lepra bacilli in the skin and nasal mucosa and in half the specimens of gland lymph. Patients improve on a good diet in a leper institution, and often suffer from worms and kidney damage, the latter complicating drug treatment. Complement fixation tests were positive in 64 per cent. The blood showed high lipids and fatty acids and low cholesterol, and these changes are not much altered by chaulmoogra treatment, the use of which should be preceded by clinico-pathologic study. *L. R.*

GRIECO (Vicente). Aspectos histologicos das nevrites na lepra. [**Histology of Nerve Lesions in Leprosy.**]—*Rev. Brasileira Leprologia.* S. Paulo. 1936. Sept. Vol. 4. No. 3. pp. 271–305. With 25 figs. [12 refs.] English summary.

Those interested in the pathological histology of leprosy will find much of interest in this article. The author is in the fortunate position of having abundant pathological material at his disposal and he clearly makes good use of it. He describes first the lesions of the nerves as found in the usual nodular form of the disease. In these he finds the bacilli numerous among the nerve fibres bringing about compression and secondary destruction. Next, in cases of purely nervous leprosy, he finds between the fibres small foci of infiltration with numerous lymphocytes and at a later stage fibrosis ; bacilli are very scarce, and in some cases lime salts are deposited. Thirdly, in the nerves of tuberculoid lesions, infiltration of epithelioid cells is seen in the nerve fibres, together with lymphoid and giant cells, caseation and calcification may occur, but Hansen's bacilli are very scarce and in many cases none can be found. Lastly, lesions of the nerve terminals in maculae, lepromata, etc. Here small infiltrations may be visible in the sheath in the early stages ; later the filament itself is invaded and the fibre compressed and ultimately destroyed. There are good photomicrographs illustrating the conditions present. *H. H. S.*

ERMAKÓVA (Nina). Studies on Leprosy. I. The Central, Sympathetic and Peripheral Nervous Systems.—*Internat. Jl. Leprosy.* Manila. 1936. July–Sept. Vol. 4. No. 3. pp. 325–336. With 5 figs. on 1 plate. [14 refs.]

WANSER (Robert). Ueber die Eosinophilie bei Lepra. [**Eosinophilia in Leprosy.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Nov. Vol. 40. No. 11. pp. 505–508.

The author records blood counts in 26 cases of leprosy with an eosinophilia varying from 6 to 16 per cent. in eleven of them. After

expelling by treatment worms of various kinds the count fell to normal, so an increase is due to complications. A high degree of lymphocytosis, such as 70 per cent., is also of no significance. *L. R.*

POOMAN (A.). Weitere Erfahrungen bei der Färbung von Lepra- und Tuberkelbakterien. [**Staining Tubercle and Leprosy Bacilli.**] —*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Dec. Vol. 40. No. 12. pp. 533–538.

As the result of his investigations he holds that the lepra and tubercle bacilli are not strictly alcohol- and acid-fast organisms. *L. R.*

HAZEN (H. H.), PARRAN (Thomas), SANFORD (Arthur H.), SENEAR (F. E.), SIMPSON (Walter M.) & VONDERLEHR (R. A.). **The Occurrence in Leprosy of Positive Serodiagnostic Tests for Syphilis. Report of Results obtained in an Evaluation of Serodiagnostic Tests for Syphilis in the United States.**—*Venereal Dis. Information.* 1936. Sept. Vol. 17. No. 9. pp. 253–259. [14 refs.]

This is a comprehensive study of the Wassermann group of tests on 1,017 specimens sent to each of thirteen serologists, summarized as follows :—

" 1. A total of 59·5 per cent. of the serologic reactions from leprosy patients were positive. The complement fixation tests showed 53 per cent. positive and the flocculation tests showed 62·4 per cent. positive.

" 2. The percentage of positive tests is somewhat higher among patients with advanced leprosy, or in those showing numerous organisms in the lesions.

" 3. It is still impossible to say whether the anesthetic, nodular, or the mixed form of leprosy yields the highest percentage of positive reactions.

" 4. There is a marked discrepancy in the results obtained with comparable specimens of blood sent to various serologists.

" 5. Up to the present time no evidence has accumulated to indicate that a disease caused by an acid-fast bacillus will give positive flocculation or complement fixation reactions for syphilis. It would seem logical to suggest that the entire question of the etiology of leprosy is in need of reinvestigation.

" 6. It seems apparent that yaws is not the cause of many positive serologic reactions for syphilis among lepers in the United States."

L. R.

ROSE (F. G.). **Treatment of Out-Patients at the British Empire Leprosy Relief Association Clinics in British Guiana.**—*Brit. Guiana Med. Ann. for 1936.* pp. 78–82.

Since the passage of the new British Guiana ordinance, for the first time limiting compulsory segregation to open bacteriologically positive cases, an increasing number of early cases have been treated at clinics, the initial cost of which was provided by the British Empire Leprosy Relief Association. In this paper Dr. Rose records the results of systematic treatment carried out in them up to approximately six years with increasing intervals between the doses, and he compares the results in these early cases with those of RODRIGUEZ in the Philippines, who considered that chaulmoogra preparations had little effect in the early neural cases which formed the great majority of Rose's cases. Dr. Rose classes as " arrested " cases those in which the lesions have disappeared and remained absent for two years, as " much improved "

those in which most of the symptoms have disappeared, and cases with a lesser degree of progress as "improved." He emphasizes that in his experience regularity of treatment is as important as its duration; 113 early cases are analysed on the lines of RODRIGUEZ, and in a second table 73 cases are given showing the degree of regularity of treatment by dividing them into those that received up to 60 per cent. of the course of injections advised and those receiving from 61 to 100 per cent. of them. In the first class only 16·7 per cent. were "arrested" after over 48 months treatment, in the latter, receiving more regular treatment, 41·7 per cent. had become arrested after 25 to 36 months, and 71·4 per cent. after 37 to 48 months' treatment. He therefore concludes that although the number is statistically small "there is nothing in them to contradict the view that early cases treated with regularity over long periods, equally with more advanced cases, prove amenable to treatment with Hydnocarpus products."

Duration of Treatment	Regularity of treatment (percentage of expected number of injections actually received during the period of treatment).													
	0 to 61 per cent.						61 to 100 per cent.							
	Cases	Arrested	Much improved	Improved	Stationary or worse	Percentage arrested	Cases	Arrested	Much improved	Improved	Stationary or worse	Percentage arrested	Total	No. arrested
13–24 months	9	0	0	3	6	0	14	0	2	9	3	0	23	0
25–36 ,,	12	0	0	1	11	0	12	5	2	2	3	41·7	24	5
37–48 ,,	4	0	0	1	3	0	7	5	0	1	1	71·4	11	5
Over 48 months	6	1	0	0	5	16·7	9	6	0	2	1	66·7	15	7
Total	31	1	0	5	25	3·2	42	16	4	14	8	38·1	73	17

L. R.

i. DE MELLO (I. Froilano). **Treatment of Leprosy by Intravenous Injections of Pure Chaulmoogra Oil.**—Reprinted from *Med. Digest.* 1935. Aug. Vol. 3. No. 5. pp. 160–162.

ii. ——. Traitement de la lèpre d'après trois ans d'expérience personelle. [**Three Years' Experience of Treatment.**]—Copia ex 2nd volumine deliberationum IX Congressus Internationalis Dermatologorum. 4 pp.

i. The author first reports negative results from the use of vaccines of Friedman bacilli, and little benefit from either antimonial preparations or methylene blue, so he remains a decided partisan of chaulmoogra, as a result of trials among the 109 lepers in the Goa leprosarium. He has used alepol, esters, etc., but has also now given 1,380 intravenous injections of pure neutralized chaulmoogra oil without any accident. The results are very encouraging with 9 discharged cured and 20 more much or very much improved.

ii. This paper deals with the same work. *L. R.*

FLANDIN (Charles), BARANGER (Pierre) & RAGU (Jean). Essai de traitement de la lèpre par un complexe nouveau de chaulmoogra et de cholestérol, permettant l'injection intraveineuse à haute dose de dérivés chaulmoogriques. [**New Treatment by a Combination of Chaulmoogra and Cholesterol.**]—*C. R. Acad. Sci.* 1936. Aug. 31. Vol. 203. No. 9. pp. 502–504.

The authors first point out that chaulmoogra preparations have proved the most efficacious in the treatment of leprosy, but that their use by a number of workers by intravenous injection has been handicapped by the production of local and general reactions. They go on to report that Pierre Baranger has prepared a number of esters of amino-alcohol, which under certain conditions unite with cholesterol to produce remarkable, crystalline, non-haemolytic substances giving fine ultra-microscopical stable suspensions suitable for intravenous injections, and which can be sterilized at 115°C. One cc. contains 20 to 40 mgm. of the preparation. This new preparation has now been tried in 12 cases of leprosy in Paris at the Hospital Saint-Louis, 1,500 ampoules having been given with perfect tolerance by slow injection, after drawing up blood into the syringe, in doses up to 6 to 7 cc. The results show in early or acute cases arrest of the evolution of the disease, and in more advanced nerve cases a stabilization of the condition, always with a rapid disappearance of the lepra bacilli and a rapidity of action much in proportion to the dosage. Its complete harmlessness leads the authors to hope that real progress has been made in the treatment of leprosy. *L. R.*

v. ORTENBERG (Heinz). Die Verbreitung der Lepra und ihre Behandlung in den deutschblütigen Bevölkerungskreisen Süd-Brasiliens. [**Leprosy Treatment in South Brazil.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Nov. Vol. 40. No. 11. pp. 503–505. With 1 fig.

The author gives a short description of the high incidence of leprosy at Santa Cruz in South Brazil with infection of the German colony as well as the negroes. In its treatment are used chaulmoogra preparations, including calestrol, by the oral, parenteral and intravenous routes. *L. R.*

TOLENTINO (Jose G.). **How Effective is the Treatment of Leprosy with the Chaulmoogra Oil Group ?**—*Monthly Bull. Bureau of Health.* Manila. 1936. Feb. Vol. 16. No. 2. pp. 48–51.

The author first refers to the differences of opinion regarding the value of the chaulmoogra treatment of leprosy and the frequency of relapses, and then deals with his five years' experience at a Cebu Philippine treatment centre. Out of 75 patients treated at the centre after the transfer of others to Culion, 37, or 50 per cent., were already paroled and 12 per cent. more were in the negative list, and another 29 per cent. were improved, and only 3 per cent. worse. Three of the paroled cases had relapsed. The present treatment therefore is very far from being useless. *L. R.*

COLE (Howard Irving) & CARDOSO (Humberto T.). Estheres ethylicos de chaulmoogra. [**Ethyl Esters of Chaulmoogra.**]—*Rev. Brasileira Leprologia.* S. Paulo. 1936. Sept. Vol. 4. No. 3. pp. 333–340. With 1 chart. English summary (8 lines).

"The factors involved in esterification of chaulmoogra oils are discussed, including experiments on the influence of sulphuric acid as a catalyst on reaction rate. The variation of refractive index and optical rotation of ethyl esters with percentage of free fatty acid is demonstrated.

"Methods of esterification and purification of ethyl esters are given as well as directions for the preparation of creosoted and iodized esters."

VAN BREUSEGHEM (R.). Le solganal associé aux ethyl esters de chaulmoogra dans le traitement de la lèpre. [**Solganal and Chaulmoogra Esters in Leprosy.**]—*Ann. Soc. Belge de Méd. Trop.* 1936. Sept. 30. Vol. 16. No. 3. pp. 379–386.

In view of the advocacy of this treatment by European workers the author reports on 15 cases in which he tried it in total quantities of solganal up to over four grams, combined with chaulmoogra esters, without obtaining any amelioration of the condition in a single case, and in all but one the disease slowly increased. *L. R.*

POOMAN (A.). Zur spezifischen Leprabehandlung mit Kohlensäureschnee und Solganal B oleosum. [**Solganal B Oleosum Treatment.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Oct. Vol. 40. No. 10. pp. 465–470.

This author, however, once more advocates solganum in oil in the treatment of leprosy, and gives a table of blood counts made during its administration. *L. R.*

TALEC & MONTGLOND. De l'influence de l'acidité de l'huile d'Hydnocarpus wightiana dans le traitement de la lèpre. [**Acidity of Hydnocarpus Oils.**]—*Ann. de Méd. et de Pharm. Colon.* 1936. July–Aug.–Sept. Vol. 34. No. 3. pp. 460–471.

The authors consider that the active principle of chaulmoogra oils has not yet been established, and quote the opinion of STEVENEL that it is localized in the integuments of the grains. They therefore consider it advisable to administer the whole oil rather than the more generally used soluble derivatives from it. The acidity of the whole oil is of importance on account of rancid preparations containing excess of acidity, but that extracted from fresh ripe seeds of *Hydnocarpus wightiana* (as long used by E. MUIR for injection purposes) is nearly neutral, for its acidity measures only 2·5 to 5·0 of oleic acid. This may be mixed in the proportion of 200 grams with 90 grams of powdered gum arabic, 250 of simple syrup and 1,000 grams of "Lixiviation de café torréfié." Two cc. of this emulsion containing 4 grams of Hydnocarpus oil.

Encouraging results are claimed to have been obtained in the treatment of a large number of patients by oral administration. In Pondicherry, 28 cases were given 30 cc. each morning, and 21 continued this dose for thirty days without the least sign of intolerance, and in most slight alleviation of their symptoms was obtained. Subcutaneous and intramuscular injections of the pure oil have also been used for over 4,000 injections with no accidents. *L. R.*

BERNY (P.) & GIPPET (E.). Essai de traitement des ulcérations lépreuses au moyen de badigeonnages quotidiens avec une solution de bleu de méthylène au centième. [**Methylene Blue in Ulceration.**]—*Bull. Soc. Path. Exot.* 1936. Oct. 14. Vol. 29. No. 8. pp. 851–854.

The authors advise the application of a solution of 1 per cent. of methylene blue to heal leprous ulcers unaccompanied by necrosis of bones. *L. R.*

MONTEL (R.) & MONTEL (G.). Suite de quelques observations de lépreux publiées en 1932. [**Further Observations on Cases.**]—*Bull. Soc. Path. Exot.* 1936. Oct. 14. Vol. 29. No. 8. pp. 857–859.

These writers report further on three cases treated in 1932 by collobiase chaulmoogra. [See MONTEL (M. L. R.), this *Bulletin*, 1932, Vol. 29, p. 848.] The cases were tropho-neuritic and tuberculoid and all the symptoms disappeared and have remained absent. *L. R.*

TISSEUIL (J.). De l'action de la sanedrine-renaleptine, associées, dans les névralgies lépreuses. [**Sanedrine-Renaleptine for Leprous Neuralgias.**]—*Bull. Soc. Path. Exot.* 1936. Oct. 14. Vol. 29. No. 8. pp. 854–856.

The author reports favourably on the suggestion of JEANSELME to use adrenaline and ephedrine in treatment of the neuralgic pains of leprosy. He uses ampoules containing 0·02 gm. of sanedrine and 0·0002 gm. of renaleptine injected daily for ten days, and repeated if necessary after a week or two interval. Four cases are recorded to illustrate its value. *L. R.*

VAN BREUSEGHEM (R.). Iode per os en thérapeutique antilépreuse. [**Iodine Therapy.**]—*Ann. Soc. Belge de Méd. Trop.* 1936. Sept. 30. Vol. 16. No. 3. pp. 367–377.

The author has tested the claims of J. BARTMAN to have obtained good results in the treatment of leprosy by a 10 per cent. alcoholic solution of iodine. The present author has given from 20 drops to 3 cc. daily of 10 grains of iodide dissolved in 100 cc. of 95 per cent. alcohol for two and a-half months on six out of seven days, the course being repeated twice after intervals of ten and fifteen days. Although the treatment was well tolerated the results have been very unsatisfactory, with strong aggravation of the symptoms in 3, moderate aggravation in 8, slightly so in 7, and the remaining 4 of the 22 treated were stationary. *L. R.*

BERTELLOTTI (L.). Tentativi di inoculazione della lepra umana nei ratti in avitaminosi. [**Results of Inoculation of Human Leprosy Tissue into Rats on Various Diets.**]—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1936. Oct. Vol. 17. No. 10. pp. 577–609. With 12 figs. [62 refs.]

The investigation undertaken was a laborious one, but the number of animals used was small. Eight groups of white rats, none of more than three, and sometimes two only, were inoculated with 1 cc. of an emulsion of human leproma in physiological saline beneath the skin of the

abdomen, into the skin of the ear and subcutaneously in the back. The animals were killed after, as a rule, 30, 60 and 90 days respectively and the tissues examined. The groups were given different diets: I. Normal for control; II. Avitaminosis A, Steenbock's diet; III. The same with the addition 3–5 drops of vogan daily (a synthetic product of vitamin A containing 40,000 units per cc.); IV. Avitaminosis B and C *plus* vitamin C ($\frac{1}{4}$ tablet of cebion); V. The same *plus* vitamin B (30 gm. dried yeast daily); VI. Avitaminosis C *plus* vitamin C; VII. Avitaminosis D; VIII. The same *plus* vitamin D (5 drops of vigantolo daily).

The results may be summarized by saying that avitaminosis did not, in these experiments, appear to bring about any reduction of defensive power or render possible the growth and propagation of leprosy; though the bacilli could be found even 90 days after inoculation they were usually undergoing degeneration. Occasionally signs indicative of multiplication were seen, but not sufficiently often to lead one to think that the conditions of the experiments played any active part.

H. H. S.

SELLARDS (M. A. W.) & PINKERTON (H.). Résumé d'expériences sur la propagation de la lèpre murine et humaine à des animaux considérés comme réfractaires. [**Propagation of Rat and Human Leprosy in Other Animals.**]—*Bull. Soc. Path. Exot.* 1936. Oct. 14. Vol. 29. No. 8. pp. 847–851.

The authors have obtained the following important results from the investigations recorded in this short paper. Progressive and fatal infections with rat leprosy have been obtained in *Macacus rhesus* monkeys, rabbits and white mice. Rapid development of the disease following injection of rat leprosy bacilli into the brain or spleen. Histological studies showed that the bacilli multiplied solely in the cytoplasm of the reticulo-endothelial system.

Attempts to propagate human lepra bacilli in mice did not give encouraging results, but in the case of the monkey moderate numbers of acido-resistant bacilli were found after two passages and two years after the first inoculation. Extensive lesions have, however, never been observed either at the site of inoculation or in distant organs.

L. R.

LAMPE (P. H. J.), DE MOOR (C. E.) & VAN VEEN (A. G.). Rattenlepra. [**Rat Leprosy.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1936. Sept. 1. Vol. 76. No. 35. pp. 2204–2227. With 9 figs. on 2 plates. English summary.

The authors have carried out experiments to try to ascertain if the virus of rat leprosy is present as a saphrophyte in the soil. In all, 95 white rats have been kept in contact with mud from native houses with heavy rat leprous infection after shaving their bellies to the point of bleeding weekly. In some the mud was well rubbed into the skin of the abdomen eight times, and some of the rats were kept on low vitamin diets, with a high mortality among them. Nearly 300 rats used for dietetic experiments without being shaved served as controls. Microscopical examinations of the skin of the abdomen sometimes

showed acid-fast rods with a morphology different from that of rat leprosy bacilli, so evidently saprophytic. In eleven rats, however, characteristic lesions of rat leprosy were found, and in a few periglandular, subcutaneous and skin lepromata were met with, and also a miliary development in enlarged internal organs, which gave the impression of being rat leprosy. Such lesions were only found after twelve months and ulceration and cachexia might supervene. B and B_2 hypovitaminosis appears to be necessary to produce infection. The infection was easily conveyed to adult rats subcutaneously or percutaneously, and the organism could not be cultivated. The control experiments were negative. In view of the necessity for lack of vitamin B complex for infection it appears unlikely that infected mud plays any great part in the natural spread of rat leprosy. *L. R.*

WATANABE (Yoshimasa). **Experimental Studies on Animals concerning Leprosy. Report VII. Filtration Tests of Virus of Rat Leprosy.**—*Kitasato Arch. Experim. Med.* 1936. Oct. Vol. 13. No. 4. pp. 348–353.

After reference to the work of MARKIANOS and others in passing the virus of rat leprosy through Chamberland L_2 filters, the author describes confirmatory experiments with that filter and possibly with L_3, but negative from the use of the Berkefeld filter. *L R.*

TERADA (M.), TERADA (Y.) & NOZAKI (M.). **Studies concerning Human and Rat Lepra Bacilli and the Other Acid Fast Organisms. Part I. Biological Studies on Human and Rat Lepra Bacilli.**—*Kitasato Arch. Experim. Med.* 1936. Oct. Vol. 13. No. 4. pp. 333–347. With 10 figs. on 2 plates.

The authors separated both human and rat leprosy bacilli from tissues containing them in large numbers by mincing and centrifuging so as to separate the bacilli in a layer, and then repeatedly washed them. They then carried out the following biochemical tests with both varieties of organisms and obtained precisely similar reactions with each. Thus both gave catalase and lipase reactions, and neither gave oxydase, protease (caseinase), or amylase ones, and neither organism fermented monosaccharides, such as glucose, galactose and levulose.

L. R.

EMERSON (George A.). **Glucose Tolerance in Rat Leprosy.**—*Amer. Jl. Trop. Med.* 1936. Nov. Vol. 16. No. 6. pp. 699–703. With 2 figs. [10 refs.]

After quoting previous work showing little or no alteration in the normal blood sugar curve in uncomplicated human leprosy, the author goes on to record experiments on well developed rat leprosy produced by infecting white rats, with the result that he found slightly decreased fasting blood sugar and abnormally high and prolonged glucose tolerance curves in advanced rat infections. This indicates more extensive damage to the liver in the rat than in human leprosy infections. *L. R.*

CHORINE (V.). Essais du traitement de la lèpre murine. [**Treatment of Rat Leprosy.**]—*Bull. Soc. Path. Exot.* 1936. Nov. 18. Vol. 29. No. 9. pp. 949–952.

In this brief note the author records negative results from attempts to treat rat leprosy with aminophenilsulfamides of M. Fourneau, with thymol and menthol, with anthiomaline, which aggravated the infection, and with selenium. *L. R.*

YAMAMOTO (Kinzaburo), SATO (Masaru) & SATO (Yuzo). Rattenlepra: Statistische Beobachtungen in Tokyo. [**Rat Leprosy in Tokyo.**]—*Japanese Jl. Dermat. & Urol.* 1936. July 20. Vol. 40. No. 1. p. 28.

The authors record the results of the microscopical examination of 2,573 rats in Tokyo for leprous lesions with 32, or 1·24 per cent., of positive results. Acid-fast bacilli were found in the subcutaneous tissues, lymph-glands, nodules, and ulcers. In 29 of the 32 it was the *Rattus norvegicus* that was infected and in the remaining 3 in the *hivernicus* variety of that rat, but no infections were met with among 39 *Rattus rattus*. Of the glands the inguinal and axillary were most often infected, and of the internal organs the lungs, liver and spleen.

L. R.

DYSENTERY.

KESSEL (John F.), BLAKELY (Lee) & CAVELL (Korine). **Amebiasis and Bacillary Dysentery in the Los Angeles County Hospital 1929–1935.** —*Amer. Jl. Trop. Med.* 1936. July. Vol. 16. No. 4. pp. 417–430. With 2 figs. [14 refs.]

This article records the results of an interesting study and one of considerable practical importance from an epidemiological point of view. The work was carried out at the laboratory of the Los Angeles County Hospital between May 1932 and September 1935, stools from dysenteric or diarrhoeic patients or swabs obtained at sigmoidoscopic examinations being sent at once to the laboratory, where cyto-diagnosis and cultural attempts were made. *E. histolytica* was found in 319 (the average number of examinations per patient was three), dysentery bacteria in 922, Salmonella in 422, of over 10,000 patients. The Shiga organism was found in 38 only (over a longer period of six years, 1929–35), Flexner V in 518, the Y bacterium in 117, and the Sonne type in 249. Of the Salmonella, *S. morgani* was the most frequent, 276.

The following table is interesting from the clinical aspect :

Gastro-intestinal symptoms in individuals harbouring E. histolytica, *Shigella and Salmonella.*

Infection	Acute dysenteric symptoms	Chronic colitis without dysentery	Without subjective gastro-intestinal symptoms
	per cent.	per cent.	per cent.
*E. histolytica,** 319 cases ...	25	61	14
Shigella paradysenteriae, 694 cases	84	12	4
Salmonella, 246 cases... ...	72	16	12

* Twenty-nine cases of amoebic liver abscess among 319, or 9 per cent.

From this it will be seen that acute bacillary dysentery is much more frequently seen than acute amoebic, while chronic amoebiasis is more common than chronic bacillary dysentery. A special study was undertaken of an outbreak of Sonne dysentery which occurred in November 1932 and May–July 1934, in Southern California. It was found but seldom prior to this and also subsequently. In the case of the organism isolated, although the serological reactions were clear, lactose fermentation was much slower and less regular than usual and in comparison with five other strains. Fermentation occurred first under anaerobiosis, in Durham tubes of lactose broth or at bottom of a lactose agar slope. Without the Durham's tube fermentation occurred more frequently in nutrient broth than in the dibasic phosphate peptone medium. *H. H. S.*

PANG KUO-HAO. Die Bedeutung der Dysenterie für China und ihre Bekämpfung. [**Dysentery in China and its Prevention.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Oct. Vol. 40. No. 10. pp. 440–448.

A good account of the main features of amoebic dysentery as it affects China, dealing with its history, its geographical and seasonal

distribution, epidemiology, symptomatology, treatment and prophylaxis. The author thinks there is evidence of the disease existing there 3000 years ago; the distribution is widespread; in fact, the disease is endemic over practically the whole of China and at times assumes epidemic proportions. Of more importance is the chronic form with complications, notably, of course, hepatitis and abscess of the liver. Amoebiasis of animals—pigs in the north, cats and dogs in the south—must be taken into consideration in the investigation of the epidemiology. Prophylaxis must be along the usual lines of better hygiene and sanitation generally, improvement of the primitive methods of fertilization, and fly-prevention. For treatment, emetine, yatren, and certain plant products such as *Garcina mangostana*; there is a great need of cheaper methods. *H. H. S.*

ROBIC (J.). Note sur la dysenterie bacillaire à Madagascar, ses rapports avec les autres dysenteries. [**Bacillary and Other Forms of Dysentery in Madagascar.**]—*Bull. Soc. Path. Exot.* 1936. Dec. 9. Vol. 29. No. 10. pp. 1126–1131.

The statement has been made that in Madagascar dysenteric diarrhoea has been observed in association with helminthic infestations —Schistosoma, Ancylostoma, Ascaris and Trichuris—and with amoeba, but that attempts to isolate any bacilli of dysentery were negative.

The author reports that in an outbreak at the beginning of 1928 *Bact. shigae* and the Hiss organism were isolated. In 1933, GIRARD concluded that bacillary dysentery was widespread fairly generally throughout the Colony. In Antananarivo, in 1934, ten positive were found, two of them Europeans, in 1935, seven in all, two Europeans, in 1936, two in the first two months. Of a total of 21 positive by agglutination, 9 reacted with Hiss' organism, 3 with the Flexner and the remainder with Shiga's.

E. histolytica was found in 7 cases of acute intestinal disturbance in 1934, six of them being in Europeans, in 1935, thirty-three positive, 26 being Europeans, and for the first six months of 1936, fifteen positive, 12 Europeans. As regards Antananarivo cases the Europeans were all persons who had lived for some length of time on the coast but had acquired the infection in other colonies.

During 1935 the stools of 604 sharpshooters were examined, 367 Madagascans and 237 Senegalese. *S. mansoni* ova were found in 19 of the former (5 per cent.) and one of the latter; none had shown any clinical signs of disease. At Vatomandry 2,123 stools were examined and the ova were found in 759, or 35 per cent.; the percentage was lowest (15) in the cool season, highest (52–54) in the hot. In the province of Ambositra the probable intermediate host is *Planorbis madagascariensis*, which resembles in some respects *P. pfeifferi*.

H. H. S.

AWAKJAN (A.). **Rats as Carriers of Dysenteric Entamoebae.**—*Rev. Microbiol., Epidémiol. et Parasit.* 1936. Vol. 15. No. 1. [In Russian pp. 23–24. English summary p. 24.]

——. **Rats as Carriers of Balantidium.**—*Ibid.* [In Russian pp. 25–26. English summary p. 26.]

In the first of these papers the author records the occurrence in 5 of 400 rats examined in Moscow of entamoebae having the characters

of *E. histolytica.* These were cultivated and were found to produce characteristic four-nuclear cysts. Injected *per rectum* in cats the amoebae proved to produce ulcerative colitis.

In the second paper it is noted that 8 of 27 rats caught in the elephant house of the zoological gardens harboured ciliates morphologically and culturally indistinguishable from *Balantidium coli* and *B. suis.* Faeces of infected rats and cultures injected rectally to rats and guineapigs produced infection in 8 of 12 experiments. The rat ciliate is named provisionally *Balantidium ratti.* Rats and guineapigs were experimentally infected with *B. coli* and rats with *B. suis.*

C. M. Wenyon.

CRAIG (Gladys M.). **A Modification of Cleveland's Medium for** *Entamoeba histolytica.—Arch. f. Protistenk.* 1936. Vol. 87. No. 2. pp. 296–298.

The short communication describes the improvement which is brought about in Cleveland's amoeba medium by diluting the human serum with sterile buffer mixture (1 in 10) before it is poured over the agar slopes. The actual agar is a mixture of Difco Bacto liver infusion agar 30·0 gm., dibasic sodium phosphate 3·0 gm., in distilled water 1·0 litre. This buffered medium with initial pH of 7·4 has constantly given heavy growth of *E. histolytica.* *C. M. W.*

DESCHIENS (R.). Action comparée du sérum de lapin et du sérum de cheval sur les cultures de l'amibe dysentérique. [**Comparison of the Action of Rabbit and Horse Serum on Cultures of the Dysentery Amoeba.**]—*C. R. Soc. Biol.* 1936. Vol. 121. No. 4. pp. 327–329.

——. Action comparée du sérum de chat et du sérum de cheval sur les cultures de l'amibe dysentérique. [**Comparison of the Action of Cat and Horse Serum on Cultures of the Dysentery Amoeba.**]—*Ibid.* No. 19. pp. 409–411.

For the cultivation of dysentery amoebae rabbit serum medium gives a growth about twice as rich as horse serum medium. The richness of the growth depends, however, to some extent on the amoebae themselves and probably on the associated bacterial flora.

In the second paper it is noted that cat serum medium gives a growth 1·45 times as rich as horse serum medium. Of certain sera tried the relative merits are given by the following figures :—human 4·9, rabbit 2·04, cat 1·45, horse 1. *C. M. W.*

DOPTER (Ch.) & DESCHIENS (R.). Action comparée du sérum humain normal et du sérum de dysentérique amibien sur l'amibe dysentérique en culture. [**Action of Normal Human Serum compared with that of Serum from Amoebic Dysentery Cases on the Dysentery Amoeba in Culture.**]—*C. R. Soc. Biol.* 1936. Vol. 123. No. 28. pp. 355–358.

The authors have already shown that if the liquid portion of the medium (which covers the coagulated horse serum slope), consisting usually of horse serum diluted with Ringer's solution, be made of human serum, the dysenteric amoebae will grow about five times more luxuriantly. In the present paper they describe experiments in

which normal human serum is compared in this respect with serum from cases of *Entamoeba histolytica* infection. The result has been to show that normal serum gives on an average 2·57 times the growth given by the serum of the cases. For an explanation of the inhibiting effect of the serum of the amoebic cases further research is required.

C. M. W.

BIRCH-HIRSCHFELD (Luise). Die Bedeutung physikalischer Bedingungen bei der Kultur der *Entamoeba histolytica*. [**Importance of Physical Conditions in the Culture of** *E. histolytica*.]—*Ztschr. f. Hyg. u. Infektionskr.* 1936. May 14. Vol. 118. No. 3. pp. 361–368. With 13 figs.

By the use of cover glass cultures of *Entamoeba histolytica* it has been possible to observe the influence of various factors on the amoebae. The amoebae in liquid culture medium are placed between a slide and cover glass, the latter supported by wax feet. The height of the cover glass is such that fluid can be passed through the culture without the amoebae being dislodged or washed away. It was found the amoebae would tolerate an osmotic pressure of from 1·4 to 0·4 times that of normal Ringer solution. Amoebae exposed to pH of 2·9 or pH 9 for several hours were still capable of recovery. Though the amoebae could survive very low oxygen pressure, they reproduced well in an atmosphere of air, the growth being greatest at the edges of the cover glass. The surface tension of the amoebae is very low, hence the susceptibility of the surface to changes in medium and the death of many cells when subcultures are made. In the cover glass cultures the behaviour of the amoebae towards red blood corpuscles and the stages of ingestion of these can be conveniently studied. *C. M. W.*

CRAIG (Gladys M.). **Relation of Hydrogen Ion Concentration to Growth and Encystment of** *Entamoeba histolytica* **in Cultures.**—*Amer. Jl. Hyg.* 1936. Jan. Vol. 23. No. 1. pp. 114–121. [12 refs.]

The paper describes a buffered medium (liver agar slope covered with buffered dilute human serum) in which *E. histolytica* grows more readily than in unbuffered media. An initial pH of 7·4–7·6 was found to be most favourable. *C. M. W.*

DESCHIENS (R.) & FLYE SAINTE-MARIE (P. E.). Comportement des cultures de l'amibe dysentérique en présence de certaines eaux d'égout. [**Cultivation of Dysentery Amoebae in the Presence of Sewer Water.**]—*C. R. Soc. Biol.* 1936. Vol. 122. No. 24. pp. 1032–1034.

The authors have shown that certain sewer waters can replace Ringer's solution in the coagulated horse serum rice starch medium for the cultivation of dysentery amoebae. By suppression of the ingredients or the addition of others (cooked or powdered beef) they have reached the conclusion that under certain conditions the sewer waters of Fez at a temperature of 32° to 37°C. are suitable for the development and encystment of the amoebae. *C. M. W.*

STONE (William S.). **A Method of producing Encystment in Cultures of** *Endamoeba histolytica.*—*Amer. Jl. Trop. Med.* 1935. Nov. Vol. 15. No. 6. pp. 681–684.

——. **Bacteria-free Antigen for the Complement-Fixation Test in Amebiasis. Preliminary Report of a New Method of Preparation.**—*Ibid.* pp. 685–687.

The method described consists essentially in transferring amoebae from a 48-hour-old culture of *E. histolytica* on Boeck-Drbohlav medium into a nutrient poor medium consisting of Locke's solution to which sterile whole wheat powder has been added. During the first 24–36 hours the introduced amoebae (from about three tubes of the original culture) will increase greatly in number, but after 48–72 hours practically all the amoebae will have encysted. A single culture will contain about 2,000,000 cysts. The cysts are normal in appearance and practically every one contains at first chromatoid bodies. These gradually disappear from the cysts, so that at the end of 14 days only an occasional cyst will be found with them. Cysts obtained in this manner have been stored in the ice-box for 4 months and have then excysted when introduced into fresh Boeck-Drbohlav medium.

In the second paper the author shows how the cysts in cultures made in the above manner may be washed and ground in alcohol to give a practically bacteria-free stable antigen which can be employed with satisfactory results for complement fixation tests. The reaction appears to be specific and does not give cross fixation with luetic and other sera. The serum of rabbits immunized by the intraperitoneal injection of four million washed live cysts gives a very clear-cut reaction with the antigen. *C. M. W.*

STONE (William S.). **A Method of eliminating** *Blastocystis hominis* **from Cultures of** *Entamoeba histolytica.*—*Jl. Lab. & Clin. Med.* 1935. Nov. Vol. 21. No. 2. pp. 190–191.

The technique described consists in adding to the supernatant fluid of a culture in Boeck-Drbohlav medium sufficient 1 in 10,000 neutral acriflavine in Ringer's solution to give a concentration of 1 in 50,000 ; after further incubation for 24 hours subculture is made and the process repeated. The amoebae are then inoculated into a medium in which the Ringer's fluid is replaced by a modified Locke's solution containing lactic acid. After several subcultures in this medium blastocystis will in most cases have entirely disappeared. *C. M. W.*

IVANIĆ (Momčilo). Zur Kenntnis der Entwicklungsgeschichte von *Entamoeba histolytica* Schaudinn. [**Development of** *E. histolytica.*] —*Zent. f. Bakt.* I. Abt. Orig. 1936. July 6. Vol. 137. No. 1/2. pp. 65–91. With 2 double plates. [24 refs.]

From a study of *E. histolytica* in a case of amoebic dysentery the author finds that the nuclear structure is very variable, that nuclear division may be promitotic or mitotic with or without the formation of chromosomes, which are six in number, and that resting stages occur which usually are seen with three nuclei. These nuclei have been evolved from the original amoebic nucleus by a complicated series of mitotic or promitotic divisions followed by degeneration of certain products of division. The three nuclei usually seen are destined to be

reduced to one by further nuclear degeneration. The whole process described and illustrated is exceedingly complicated and the reviewer feels that much more evidence than that produced by the author will be necessary before his views can be accepted. *C. M. W.*

DESCHIENS (R.). Perte de la virulence de deux souches d'amibes dysentériques en culture. [**Loss of Virulence of Two Strains of Dysentery Amoebae in Culture.**]—*Bull. Soc. Path. Exot.* 1936. May 13. Vol. 29. No. 5. pp. 576–584. [14 refs.]

Two strains of dysentery amoebae which were pathogenic both to man and to the cat were found to have become non-pathogenic after culture for 90 to 170 days in one case and for 302–352 days in the other. The pathogenicity was tested on twenty animals by direct inoculation into the ileum through an abdominal incision according to the technique of Meleney and Frye. *C. M. W.*

DESCHIENS (R.). Modifications expérimentales du pouvoir pathogène de l'amibe dysentérique. [**Experimental Modifications of the Pathogenicity of the Dysentery Amoeba.**]—*C. R. Soc. Biol.* 1936. Vol. 123. No. 32. pp. 783–785.

Strains of *Entamoeba histolytica* which by long culture have lost much of their pathogenicity for kittens, as tested by inoculation of culture into the ileum after laparotomy, are liable to prove more pathogenic if bacteria from other and more virulent cultures or suspensions of killed typhoid or paratyphoid organisms are added to the inoculum. This result rather suggests that the flora associated with the amoebae are important in determining the pathogenicity.

C. M. W.

MELENEY (Henry E.) & FRYE (William W.). **The Pathogenicity of** *Endamoeba histolytica.—Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. Jan. 25. Vol. 29. No. 4. pp. 369–379. [25 refs.]

By adopting a uniform method of culture of *E. histolytica* and technique of inoculation into a standard number of kittens the authors have tested the pathogenicity of various strains of dysentery amoebae. The conclusion is that variations in the clinical picture appear to depend first on the resistance of the hosts and secondly on the pathogenic activity of different strains of the amoeba. It has not seemed that prolonged cultivation has decreased the pathogenicity of any strain. It has not been found possible to raise the pathogenicity of any strain. A strain of *E. histolytica* in any population group appears to remain fairly constant as regards pathogenicity provided there is little chance of introduction of fresh strains into the group from without. In medical practice any strain should be regarded as dangerous.

C. M. W.

FRYE (William W.) & MELENEY (Henry E.). **The Effect of Various Suspending Media on the Pathogenic and Phagocytic Activity of** *Endamoeba histolytica.—Amer. Jl. Hyg.* 1936. Sept. Vol. 24. No. 2. pp. 414–422.

In a previous communication the authors reported that the pathogenicity of *E. histolytica* for kittens appeared to be reduced if the

amoebae, before inoculation, were washed free of the bacteria which accompany them in the cultures and then suspended in horse serum–Ringer (1 : 6). It was thought that the result was probably due to the removal of the bacteria. A series of experiments here reported show that the horse serum was the cause and not the removal of the bacteria. Ringer's solution alone, without horse serum, has no such effect, while Ringer with boiled horse serum appeared to increase the pathogenicity of the amoebae as also did the filtered and boiled fluid from an amoeba culture in which, furthermore, the *in vitro* phagocytosis of red blood cells by the amoebae was most marked. *C. M. W.*

TER-MATEVOSSIAN (S.), SARKISSIAN (M.) & ZATURIAN (A.). [**The Pathogenicity to Kittens of Strains of** *Entamoeba histolytica* **occurring in Armenia.**]—*Med. Parasit. & Parasitic Dis.* Moscow. 1936. Vol. 5. No. 1. [In Russian pp. 108–118.]

The authors tested the virulence for kittens of four strains of *Entamoeba histolytica* isolated in culture from cases of distinct forms of amoebiasis in Armenia : one of acute dysentery ; another of untreated chronic amoebiasis ; the third of a chronic case treated with emetine, and the fourth from a symptomless carrier.

Altogether fifty-two kittens were inoculated with cultures *per rectum* and their faeces were examined daily. All the strains of amoebae used proved to be pathogenic to kittens in various degrees, the one isolated from the acute case being most virulent, those from the chronic cases less so, and the one from the " carrier " case the least.

C. A. Hoare.

ZATURJAN (A.). Ueber nicht pathogene histolytica-ähnliche Amöben. [**Non-pathogenic** *histolytica*-**like Amoebae.**]—*Rev. Microbiol., Epidémiol. et Parasit.* 1936. Vol. 15. No. 1. [In Russian pp. 60–65. With 12 figs. German summary p. 66.]

During the study of strains of *E. histolytica* in Armenia an amoeba was seen which reached a diameter of 17 microns and produced cysts 7–14 microns in diameter and characterized by the presence of numerous chromatoid bodies and a single nucleus. The amoeba was cultivated but did not produce cysts in culture. It was not possible to infect kittens. It is thought that a new species of *Entamoeba* may be represented, but further cases of the infection are being looked for.

C. M. W.

BONNIN (H.) & COURDURIER. La culture d'*Entamoeba histolytica* et ses applications cliniques. [**Culture of** *E. histolytica* **and its Clinical Applications.**]—Reprinted from *Maroc-Méd.* 1936. June 15. No. 168. 31 pp. [5 pages of refs.]

—— & ——. La culture d'*Entamoeba dysenteriae* et ses applications cliniques.—Abridged version of above : Reprinted from *Gaz. Méd. de France.* 1936. Vol. 43. No. 14. 18 pp.

In these articles the authors review the development of the cultivation of *Entamoeba histolytica* since this was first satisfactorily carried out by BOECK and DRBOHLAV in 1924. The media which have been employed

and the uses to which the cultures have been put are fully discussed and it is concluded that the culture methods are still hardly applicable to the routine laboratory diagnosis of amoebic infections. The use of amoebae from cultures for preparation of antigens for complement fixation tests is still in the experimental stage, while the culture methods have not yet settled the question as to whether there are pathogenic and non-pathogenic races of *E. histolytica.* *C. M. W.*

CRAIG (Charles F.). **Some Unsolved Problems in the Parasitology of Amebiasis.**—*Jl. Parasitology.* 1936. Feb. Vol. 22. No. 1. pp. 1–13. [51 refs.]

In this paper, the address of the retiring president of the American Society of Parasitologists, the author discusses the possibility of the existence of a completely non-pathogenic race of *E. histolytica* (*E. dispar* of Brumpt), the question of the existence of races of *E. histolytica* of varying virulence and the subject of immunity after amoebic infections. The answer to the first question is not known, that to the second in the affirmative, while that to the third cannot be given, as the evidence is insufficient in spite of the knowledge that specific complement-fixing bodies occur in the blood of animals and individuals infected with *E. histolytica.* *C. M. W.*

SPECTOR (Bertha Kaplan). **Significance of the Small Variety** *Endameba histolytica.*—*Amer. Jl. Public Health.* 1936. Aug. Vol. 26. No. 8. pp. 813–818. With 1 fig. [12 refs.]

In the summer of 1933, when the Chicago epidemic of amoebic dysentery started, the race of *E. histolytica* producing small cysts (5 μ or less up to 12 μ) was not encountered. It first appeared in December 1933 and soon assumed a prominent rôle, reaching its height in June 1934 and then declining till December 1934. It increased in frequency during January, February and March 1935, and has declined steadily since then, so that at the time of writing it was difficult to get a heavily infected specimen. A series of experiments designed to compare the small race with the ordinary one was arranged. It was found that the small race was more difficult to cultivate but that in the culture the amoebae were either small or larger, reaching the size of the amoebae in cultures of the large race. With antigen prepared from the large race amoebae the serum of cases infected with the small race could not be shown to contain complement fixing substances, whereas the serum of cases infected with the large race gave strongly positive reactions. With cysts of the small race administered by the mouth 8 of 37 kittens became infected, while 10 of 22 became infected when cysts of the large race were used. The large race given *per rectum* resulted in typical severe amoebic infection in kittens, while similar inoculations of the small race failed to produce results. Clinically in human beings the small race produces milder symptoms than the large race, rectal ulceration, pus, gross blood or evidence of organic involvement of the colon, and liver abscess being absent. Though the small race differs from the large race in these characters it is regarded merely as a race of *E. histolytica* and not as a distinct species. *C. M. W.*

BIRCH-HIRSCHFELD (Luise). Ueber die Wirkung niederer Carbonsäuren und ihrer α-Oxyderivate auf *Entamoeba histolytica.* [**Action of Lower Fatty Acids and their α-Hydroxy Derivatives on** *E. histolytica.*]—*Ztschr. f. Hyg. u. Infektionskr.* 1936. Nov. 14. Vol. 119. No. 1. pp. 91–102. With 6 figs.

By the use of microculture methods for observing the growth and movements of *E. histolytica* the author has been able to expose the amoebae to the action of organic acids and has noted that under certain conditions of pH and concentration definite cytoplasmic and nuclear degenerative changes are brought about. *C. M. W.*

FRYE (William W.) & MELENEY (Henry E.). **The Viability of** *Endamoeba histolytica* **Cysts after Passage through the Cockroach.**—*Jl. Parasitology.* 1936. Apr. Vol. 22. No. 2. pp. 221–222.

It is shown that cysts of *Entamoeba histolytica* will survive in and pass through the intestine of cockroaches. Cultures were obtained from the droppings of cockroaches passed 48 hours after feeding on cyst-containing faeces. *C. M. W.*

DEYOUNG (Willard). **Sources of Error in the Laboratory Diagnosis of Amebiasis.**—*Jl. Lab. & Clin. Med.* 1936. Aug. Vol. 21. No. 11. pp. 1149–1154. [12 refs.]

The value of the culture method as a means of diagnosis of *Entamoeba histolytica* infection was examined. It has been found that in culture *E. histolytica* and *E. coli* may come to resemble one another so closely that their differentiation in the time in which a diagnosis has to be made may be quite impossible. The culture method for diagnostic purposes may then be misleading. Reliance has to be placed on examination of fresh and fixed faecal specimens which will give an accurate diagnosis only when typical free or encysted *E. histolytica* are present. Faeces obtained after the ingestion of oil, bismuth or arsenic or by means of a saline purge are liable to lead to errors.

C. M. W.

BRUG (S. L.). Die Eosinmethode bei der Stuhluntersuchung auf Protozoen. [**The Eosin Method of Stool Examination for Protozoa.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Nov. Vol. 40. No. 11. pp. 522–523.

The author writes in favour of the eosin method of stool examination for intestinal protozoa and their cysts, as first introduced in 1913 by KUENEN and SWELLENGREBEL. The preparation is made by mixing the faeces with a 2 per cent. eosin solution. The unstained living protozoa and their cysts stand out clearly against the rose-coloured background and are thus more easily seen than in the ordinary saline or iodine preparations. *C. M. W.*

ANDREWS (Justin) & WHITE (Harry F.). **An Epidemiological Study of Protozoa Parasitic in Wild Rats in Baltimore, with Special Reference to** *Endamoeba histolytica.*—*Amer. Jl. Hyg.* 1936. July. Vol. 24. No. 1. pp. 184–206. With 2 figs. [56 refs.]

The paper has to do with the results of a survey of rats for protozoan parasites carried out in Baltimore from October 3, 1934 to October 11,

1935. More than 2,500 Norway rats received alive were examined for intestinal blood-inhabiting and other protozoa. The organisms found were *Entamoeba histolytica, E. muris, Trichomonas muris, T. parva, Chilomastix bettencourti, Retortamonas* (*Embadomonas*), *Giardia muris, Eimeria miyairii, E. carinii, E. separata, Balantidium coli, Hexamita muris, Endolimax nana, Trypanosoma lewisi, Hepatozoon muris* and *Sarcocystis* sp. Certain of these, *T. parva, T. lewisi* and the coccidia, were more common in young than in adult rats. *Sarcocystis* was exclusively a parasite of adults. The maximum incidence of coccidia was in the spring, of *T. lewisi* in the summer and of *T. parva* in the summer and autumn. Infection with *E. histolytica* was found in 28 rats. *C. M. W.*

BARBAGALLO (Bonaventura). La prova di Weltmann nelle coliti amebiche e non amebiche. [**Weltmann Test in Amoebic and Non-amoebic Colitis.**]—*Riforma Med.* 1936. May 30. Vol. 52. No. 22. pp. 743–745. [10 refs.]

The author has applied the Weltmann test, which is, in brief, the degree of coagulation brought about by heat on various dilutions of serum, to the sera of cases of amoebic and non-amoebic colitis. The finding is that in all conditions of colitis there is an increase in the coagulation band. *C. M. W.*

SHIRAOGAWA (H.). Immunologische Studie ueber die Dysenterieamöbe. [**Immunological Studies on the Dysentery Amoeba.**]—*Fukuoka Acta Med.* (*Fukuoka-Ikwadaigaku-Zasshi*). 1935. Nov. Vol. 28. No. 11. [In Japanese pp. 2635–2672. [38 refs.]; 2673–2729. With 1 chart & 65 figs. on 2 plates. [28 refs.]; 2730–2760. [17 refs.] German summary pp. 113–115.]

By alcoholic abstract of culture amoebae the author has obtained haemolytic substances which in the case of the *E. histolytica* extract were active in a dilution of 1 : 640, the *E. coli* extract being much weaker. Rabbits injected with these extracts developed immune substances which for complement fixation, precipitin and amoebalytic reactions were specific for the homologous amoebae. In a series of 23 amoebic cases similar immune bodies were demonstrated in the sera. *C. M. W.*

CRAIG (Charles F.). **The Diagnostic Value of the Complement Fixation Test in Amebiasis.**—*Rev. Parasit., Clin. y Lab.* Habana. 1936. May–June. Vol. 2. No. 3. pp. 305–314. [17 refs.]

In an earlier paper the author (1933) reviewed the results he had obtained with the test in 1,000 individuals and considered its diagnostic value. In the present paper it is stated that the tests since carried out have not materially differed from those previously reported. The conclusions reached are similar to those in the 1933 paper, to the review of which readers are referred (this *Bulletin*, 1933, Vol. 30, p. 760). *C. M. W.*

ATCHLEY (Floyd O.). **Experimental Infections of Rats with** *Endamoeba histolytica.*—*Amer. Jl. Hyg.* 1936. Mar. Vol. 23. No. 2. pp. 410–414. [13 refs.]

With *E. histolytica* strains from wild rats and from man laboratory rats have been inoculated *per os.* With the rat strain 8 out of 17 animals became infected, whereas with the human strain only 4 out of 30 experiments succeeded. Cysts were observed in only one animal which a month before had received the human strain by the mouth. The infections in both the naturally infected and experimentally infected rats produced no intestinal change. Of 6 kittens inoculated with a wild rat strain two became positive, though it was not possible to demonstrate invasion of the tissues. *C. M. W.*

ALEXEIEFF (A.). Sur le métabolisme du glycogène chez les trichomonas et les entamibes. [**Metabolism of the Glycogen in the Trichomonads and Entamoebas.**]—*Bull. Soc. Path. Exot.* 1936. Feb. 12. Vol. 29. No. 2. pp. 116–118.

During the growing phase of certain species of *Trichomonas* glycogen accumulates in the cytoplasm, especially in the neighbourhood of the axostyle. When division is taking place, during which the axostyle is absorbed, the glycogen is used up so that by the time division is complete this substance can no longer be detected.

In the case of *Entamoeba histolytica* glycogen is distributed throughout the cytoplasm of the trophozoites. When encystment occurs the glycogen is concentrated into one mass to form the well-known glycogenic vacuole. In *E. coli*, on the other hand, glycogen is not present in the cytoplasm. *C. M. W.*

SPECTOR (Bertha Kaplan). **Self-Inoculation with** *Endamoeba histolytica* **Trophozoites through Vaseline and the Longevity of the Trophozoites in Vaseline.**—*Amer. Jl. Trop. Med.* 1935. Nov. Vol. 15. No. 6. pp. 689–691.

The patient appears to have contracted amoebic infection by applying to the anus, for relief of constipation, vaseline from a jar which was used by an undoubted amoebic case to allay the anal irritation of persistent diarrhoea. It was shown subsequently that dysentery amoebae in blood and mucus smeared on vaseline will remain alive for over nine hours at laboratory temperature. *C. M. W.*

GERMAIN (A.), CARBONI (P.) & MORVAN (A.). Hémorragies intestinales intermittentes, seul signe d'amibiase chronique latente. [**Intermittent Intestinal Haemorrhage in Chronic Latent Amoebiasis.**]—*Bull. Soc. Path. Exot.* 1936. June 10. Vol. 29. No. 6. pp. 673–677.

The case of a soldier, 27 years of age, 11 years' service in South America, the coast of Africa, and Indo-China. In the course of less than two years, June 1934–February 1936, he had three attacks of haemorrhage from the bowel, in June 1934, July 1935, and February 1936, fairly profuse up to 300 gm. at a time, and smaller bleedings in January 1935 on and off for a fortnight. The only other symptom present was pain to the right of the umbilicus. Examination of the faeces revealed cysts of *E. histolytica* and by sigmoidoscope ulcers in

the sigmoid. There were no internal haemorrhoids, or polypi. A course of emetine followed by stovarsol resulted in disappearance of the cysts and healing of the ulcers. No other cause could be found for the bleeding. No history of any dysenteric attack could be obtained. *H. H. S.*

BANERJI (L. M.), CHOPRA (R. N.) & RAY (P. N.). **Amoebiasis and Appendicitis.**—*Indian Med. Gaz.* 1936. Dec. Vol. 71. No. 12. pp. 693–699. With 7 figs. on 3 plates. [15 refs.]

The incidence of appendicitis as a complication in amoebic dysentery has been noted by several observers. Thus, STRONG, in a series of 100 fatal cases of this form of dysentery found it in 7, CLARK, H. C. (*Amer. Jl. Trop. Med.* 1925, Vol. 5, p. 157) found amoebic ulcerative appendicitis in 76 out of 186 (40·8 per cent.) autopsies on cases of amoebic dysentery and 9·2 per cent. of these had resulted in perforation or abscess, and CRAIG in 1934 from analysis of 60 cases of amoebic dysentery found 16 (26·6 per cent.) with appendicitis.

The authors have studied the large number of 475 cases of appendicectomy and find in 5 per cent. an association with amoebiasis, and nearly half the patients gave a history of dysentery within the preceding year. In a series of 25 cases in which no emetine had been given cysts of *E. histolytica* were found in scrapings from the appendical mucosa. Sigmoidoscopy was a valuable diagnostic aid; in 11 out of 28 consecutive cases cysts were found in the stools and the entamoeba was found in scrapings of three. Inflammation of the submucous layers with some degree of fibrosis of the appendix was seen, but rarely the typical amoebic ulceration, probably because in most cases emetine has been given prior to the operation. In a later paper the radiological study of cases is to be dealt with. *H. H. S.*

GREPPI (E.) & DELEONARDI (S.). Anemia ipocromica achilica in amebiasi intestinale cronica.—Reprinted from *Boll. d. Soc. Med.-Chirurg. Catania.* 1935. Feb. 21. Vol. 3. No. 2. pp. 110–126. With 2 figs.

GOLDBURGH (Harold L.). **Amebic Abscess of the Liver: Report of a Case without Previous Manifestations of Amebiasis: Operation and Recovery.**—*Trans. College of Physicians of Philadelphia.* 1936. 4th Ser. Vol. 4. No. 1. pp. 46–47.

The case recorded is that of a man of 58 who was operated upon for a condition indicating acute gall bladder syndrome with probable liver complications. A solitary right lobe liver abscess, from which ten ounces of brownish pus were evacuated, was discovered. In the pus *Entamoeba histolytica* was found. Ten stool examinations failed to reveal either free or encysted amoebae, though the X-ray of the colon did show chronic inflammatory lesions at the caecum and ascending colon. The case, which gave no history of previous dysentery, illustrates the fact that the first symptoms of amoebiasis may be those of amoebic abscess of the liver. *C. M. W.*

MÜHLENS (P.) Amöbenruhr und Ruhrfolgen.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1937. Feb. Vol. 41. No. 2. pp. 245–250.

FISCHER (O.) Amöbenruhr und Ruhrfolgen.—*Arch. f. Schiffs- u Trop.-Hyg.* 1937. Feb. Vol. 41. No. 2. pp. 251–256. With 4 figs.

WENRICH (D. H.). **Studies on *Dientamoeba fragilis* (Protozoa). I. Observations with Special Reference to Nuclear Structure.**—*Jl. Parasitology.* 1936. Feb. Vol. 22. No. 1. pp. 76–83. With 25 figs. [12 refs.]

The author notes that infections with *Dientamoeba fragilis* are of more common occurrence and that the amoeba itself is capable of persistence in faeces for a longer time than is usually supposed. The nucleus contains four or more granules and it is suggested that when the number is eight this results from division of an original four granules or the fusion of two nuclei each with four granules. In the nucleus one granule larger than the others probably represents a karyosome. No true cysts have been identified, though certain individuals suggest precystic forms. *C. M. W.*

BRUG (S. L.). *Dientamoeba fragilis.—Geneesk. Tijdschr. v. Nederl.-Indië.* 1936. May 26. Vol. 76. No. 21. pp. 1288–1302. With 2 charts & 1 plate. English summary.

The intestinal protozoa of 80 inmates of an asylum in Amsterdam were investigated. All the usual forms were found but the high incidence of infection with *Dientamoeba fragilis* is noteworthy. This amoeba was demonstrated in 10 cases by direct examination of faeces and in 19 others by culture methods. It is pointed out that it is not as fragile as its name implies, a culture having been obtained from a 13½-hour-old stool. Nuclear division is described, as also the occurrence in cultures of what may be precystic forms. To obtain subcultures it was necessary to inoculate tubes with material from another tube containing at least 100 amoebae per cc. Even then there was a lag phase or marked diminution of amoebae during the first day. *C. M. W.*

HAKANSSON (E. G.). *Dientamoeba fragilis,* **a Cause of Illness. Report of Case.**—*Amer. Jl. Trop. Med.* 1936. Mar. Vol. 16. No. 2. pp. 175–185. With 16 figs. on 1 plate.

The case described is that of a physician in Panama who suffered from acute colitic irritation with diarrhoea of 14 days' duration. During this time the symptoms, which gave rise to a general feeling of illness, became very severe in character on three occasions, on each of which very large numbers of *Dientamoeba fragilis* occurred in the stools. Though the amoebae were present between the attacks they were scanty and much smaller than when they appeared to be in a condition of active cultivation in the intestine. On the 14th day carbarsone treatment (0·25 gm. 3 times a day) was commenced. On the following day there was marked improvement and no amoebae could be found. Recovery was uninterrupted, so that treatment was discontinued on the third day. The stools were examined daily for two weeks and then twice a week for 5 months without the discovery of any amoebae. There has been no recurrence of symptoms. The conclusion is that it does not seem possible that *D. fragilis* played its reputed rôle of a harmless commensal during this illness. No other protozoa were found. It is noted that though the name *fragilis* suggests a fragile amoeba, actually it is able to persist alive in stools up to 48 hours after evacuation. It is pointed out that if the living amoeba is examined in water the toughness and resistancy of the

ectoplasm causes it to rupture and evacuate its endoplasm through the ectoplasm in a manner so characteristic that this feature may be used for identification purposes. *C. M. W.*

GUPTA (B. M. Das). **A Case of Human Infection with** *Dientamoeba fragilis* **Jepps and Dobell, 1918, in Calcutta.**—*Indian Med. Gaz.* 1936. Sept. Vol. 71. No. 9. pp. 528–529. With 5 figs.

The case described is the first one to be reported from Calcutta. Some of the amoebae were remarkable for their size, reaching 16·5 microns in diameter. *C. M. W.*

GIROLAMI (Mario). L'amebiasi urinaria. Rivista critico-sintetica con contributo clinico e sperimentale. [**Urinary Amoebiasis.**]—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1936. Mar. & Apr. Vol. 17. Nos. 3 & 4. pp. 129–176; 228–246. With 6 figs. [3 pages of refs.]

This is a long article, written in a critical style, reviewing the literature of so-called urinary amoebiasis and recording certain new observations on this condition. It is concluded that the claims of PENSO that a particular species of amoeba, *Entamoeba vesicalis*, occurs in human urine and is definitely pathogenic are well founded and that both it and *Entamoeba histolytica* may be the cause of cystitis and other diseases of the urinary tract. It is claimed that both occur in urine in the free and encysted stage, but it would seem from the description and illustrations of the encysted forms that there has been no clear appreciation on the part of the author as to what constitutes an encysted stage. The reviewer cannot avoid the impression that no reliance can be placed on the observations recorded. *C. M. W.*

BACHRACH (Robert). Ueber Amöben-Infektion der Harnwege. [**Amoebic Infection of the Urinary Tract.**]—*Wien. Klin. Woch.* 1936. Sept. 11. Vol. 49. No. 37/38. pp. 1123–1125. With 2 figs.

A patient who developed haematuria four years after suffering from amoebic dysentery was found to be suffering from gonorrhoea and papilloma of the bladder. In the urinary sediment amongst numerous red blood corpuscles, leucocytes and other cells were seen certain large vacuolated cells (25–50 microns) with included red blood corpuscles and other material. In sections of the incised papilloma large cells having an average diameter of 30 microns were occasionally seen. It is concluded that these cells are amoebae but to the reviewer the evidence of their amoebic nature is not entirely satisfactory.

C. M. W.

MANOHAR (K. D.). **A Case of Urinary Amoebiasis. Review of the Literature.** [Memoranda.]—*Brit. Med. Jl.* 1936. Apr. 4. pp. 694–695. [10 refs.]

The discovery in the urine of a woman on four occasions during the course of two weeks of large sluggishly motile cells with occasional included red blood corpuscles led to the diagnosis of urinary amoebiasis. No amoebae were found in the faeces. The motile cells in the urine formed ectoplasmic pseudopodia and had nuclei of the entamoeba type.

It does not seem possible to be certain from this account that the cells were amoebae and not macrophages. *C. M. W.*

CARINI (A.). Un cas d'amibiase cutanée. Considérations sur les localisations extra-intestinales de l'amibiase et spécialement sur l'amibiase cutanée. [**Case of Cutaneous Amoebiasis. Considerations on the Extra-Intestinal Localizations of Amoebiasis and Especially on Cutaneous Amoebiasis.**]—*Bull. Soc. Path. Exot.* 1936. May 13. Vol. 29. No. 5. pp. 584–596. With 5 figs. [15 refs.]

The case recorded is that of a man who suffered from amoebic dysentery and developed a peri-anal ulcerative condition due to invasion of the skin by the amoebae. The skin condition appeared to commence after the appearance of perineal furuncles which presumably gave a passage into the skin for the amoebae. When the condition had been diagnosed by the discovery of amoebae in the tissues a rapid cure was effected by emetin injections and quinine applications locally.

C. M. W.

JOSLYN (Harold L.). **Effective Method of treating Amebic Abscess of the Liver.**—*Jl. Amer. Med. Assoc.* 1936. Dec. 26. Vol. 107. No. 26. pp. 2117–2119.

If, as the author states, the idea of treating amoebic abscess of the liver by aspiration and emetine injections is little known in most parts of the United States, then it is high time that the knowledge was made more widely accessible and the author has done well to publish details of his two cases. It is more than a quarter of a century ago that Sir Leonard ROGERS reported several cases successfully treated by aspiration, and 14 or 15 years since he showed the greater success from aspiration *plus* emetine injections. *H. H. S.*

GIOVANNI (Magliano). Amebiasi, ascesso epatico ed emetinoterapia. [**Liver Abscess treated with Emetine.**]—*Ann. di Med. Nav. e Colon.* 1936. Nov.–Dec. 42nd Year. Vol. 2. No. 5–6. pp. 237–240. With 2 charts & 1 fig.

The patient presented symptoms of abscess of the liver and was treated by emetine intramuscularly and recovered. The diagnosis was based on the results of treatment. Examination of the stools did not result in the finding of *E. histolytica* and the liver was not explored. *H. H. S.*

PECKOLT (Waldemar) & PRADO (Alcides). Contribuição á materia medica vegetal do Brasil. VI. Estudo pharmacognostico e therapeutico da *Jacaranda decurrens* Cham. (*Bignoniaceae*). [**Vegetable Materia Medica of Brazil. VI. Pharmacognosy and Therapeutics of *Jacaranda decurrens* Cham.**—*Mem. Inst. Butantan.* 1935. Vol. 9. pp. 301–318. With 3 figs. English summary (9 lines).

It is claimed that the administration of tincture of *Jacaranda decurrens* will rid the intestine of all the intestinal protozoa, including *E. histolytica.* *C. M. W.*

BOURROUL (Celestino). Tratamento das amibioses. [**Treatment of Amoebiasis.**]—*Folha Med.* 1936. Aug. 5. Vol. 17. No. 22. pp. 373–375.

This gives a list, with doses, of a large number of remedies which have been employed for the treatment of amoebiasis. *C. M. W.*

MAJUMDAR (Akhil Ranjan). Difficulties in the Treatment of Amoebiasis.—*Jl. Indian Med. Assoc.* 1936. Sept. Vol. 5. No. 12. pp. 746–752. [66 refs.]

KNAUFF (Günther). Studien ueber *Balantidium coli.* [**Studies on** *Bal. coli.*]—*Ztschr. f. Parasitenk.* 1935. Dec. 13. Vol. 8. No. 2. pp. 139–182. With 11 figs. [70 refs.]

The paper is a record of observations carried out on *Balantidium* in pigs, and culture experiments with the ciliate, which is compared with the forms recorded from man, monkeys, sheep and other animals.

C. M. W.

RACHMANOW (H.) Die Bestimmung des spezifischen Gewichts der Zysten von *Lamblia intestinalis* (*Giardia intestinalis*). [**Determination of the Specific Gravity of Cysts of** *Lamblia intestinalis* (*Giardia intestinalis*).]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Sept. Vol. 40. No. 9. pp. 395–396.

The testing of lamblia cysts with fluids of varying specific gravity has shown that they correspond to a 30 per cent. sugar solution and have thus a specific gravity of approximately of 1·1133. A three months old child was passing daily 300 to 900 million cysts. *C. M. W.*

MORENAS (L.). Les aspects cliniques de la lambliose en France. [**Clinical Aspects of Lambliasis in France.**]—*Rev. Parasit., Clin. y Lab.* Habana. 1936. May–June. Vol. 2. No. 3. pp. 445–453. English summary.

The frequency with which the flagellate lamblia is discovered in the faeces of cases of diarrhoea, especially in children, or in the material obtained by duodenal tubage is being interpreted by clinicians as evidence of its pathogenicity. A definite disease condition, lambliasis, is being visualized and various types of the infection are described—enteritic, biliary, cachectic and healthy carrier. This article sets forth this clinical point of view and discusses in some detail the symptomatology of the various types of infection. The erroneous assumption is made, as is so often the case, that the presence of flagellates in material obtained by duodenal tubage is evidence of their actual presence in the gall bladder. *C. M. W.*

SIMICI (D.), POPESCU (M.) & COVACEANU (C.). Recherches faites en Roumanie sur la fréquence de l'infection du duodénum et des voies biliaires par les lamblias intestinalis. [**Researches made in Rumania on the Frequency of Lamblia Infection of the Duodenum and Biliary Tracts.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Bucarest.* 1935. Nov. Vol. 17. No. 9. pp. 154–160.

By various methods of obtaining fluid from the duodenum and stimulating flow of bile from the bile duct the authors come to the conclusion

that *Giardia intestinalis* actually may inhabit the bile duct or gall bladder. The evidence is that the later withdrawn fluid may contain more organisms than the first. However suggestive such evidence may be, it has to be remembered that the flagellate lives within the lumen of the duodenal glands and on the surface of the duodenal epithelium, so that it seems not improbable that the flagellates seen in duodenal fluid have come from these localities and not from the bile duct. A few well authenticated cases of discovery of flagellates in the gall bladder at surgical operations, or even at post-mortem examinations, by trustworthy observers who know how to carry out such investigations would settle the much disputed question. *C. M. W.*

POZZI (A.) & DE MURO (P.). Sulla giardiasi duodenale. [**Duodenal Giardiasis.**]—*Policlinico.* Sez. Prat. 1935. Dec. 2. Vol. 42. No. 48. pp. 2359–2362, 2365–2368. [42 refs.]

The paper describes three cases of *Giardia intestinalis* infection and the symptoms associated with this. A cure was obtained by duodenal irrigation with 0·4 per cent. hydrochloric acid solution and oral administration of magnesium sulphate on alternate days. *C. M. W.*

NUNAN (Berardo). Giardiose intestinal na criança. [**Intestinal Giardiasis in Children.**]—*Brasil-Medico.* 1936. May 2. Vol. 50. No. 18. pp. 379–383. [14 refs.]

A general account of the condition which is being termed "giardia enteritis" in children. *C. M. W.*

ENAULT. Un cas de colite à lamblia chez un malade ne tolérant pas l'arsenic; traitement créno-médicamenteux; résultat.—*Marseille-Méd.* 1936. Mar. 15. Vol. 73. No. 8. pp. 329–332.

GONZÁLEZ (Gustavo). Flagelosis intestinales. [**Intestinal Flagellate Infections.**]—*Rev. Med.-Cirurg. do Brasil.* 1935. Oct. Vol. 43. No. 10. pp. 693–700.

A discussion of various symptoms and groups of symptoms which are attributed by the author to infections with *Giardia, Chilomastix* or *Trichomonas.* *C. M. W.*

YELLOW FEVER.

i. JAMES (S. P.) Renseignements sur la fièvre jaune reçus au cours des six mois finissant le 31 mars 1936. [**Information on Yellow Fever received during the Course of the Six Months ending 31st March, 1936.**]—*Bull. Office Internat. d'Hyg. Publique.* 1936. July. Vol. 28. No. 7. pp. 1267–1277. With 1 folding map. [12 refs.]

ii. SOREL. Les cas de fièvre jaune dans les colonies françaises en 1935. [**Yellow Fever Cases in French Colonies in 1935.**]—*Ibid.* pp. 1278–1291. With 1 diagram & 1 map.

iii. PRIDIE (E. D.). Faits récents concernant la fièvre jaune dans le Soudan Anglo-Egyptien, en particulier la lutte contre les moustiques. [**Recent Facts concerning Yellow Fever in the Anglo-Egyptian Sudan, especially Anti-Mosquito Measures.**]—*Ibid.* pp. 1292–1297. With 2 maps (1 folding).

iv. MEJIA (Hernández). Le test de protection et l'épidémiologie de la fièvre jaune au Mexique. [**The Protection Test and the Epidemiology of Yellow Fever in Mexico.**]—*Ibid.* pp. 1298–1308.

v. BOYÉ. Séro-vaccinations anti-amariles et recherches concernant le test de protection en Afrique Equatoriale Française. [**Serum Vaccination against Yellow Fever and Studies on the Protection Test in French Equatorial Africa.**]—*Ibid.* pp. 1309–1312.

vi. BABLET (J.). Deuxième note sur le diagnostic histologique de la fièvre jaune (examen des coupes de foie). [**A Second Note on the Histological Diagnosis of Yellow Fever. (Examination of Liver Sections.)**]—*Ibid.* pp. 1313–1320.

vii. FINDLAY (G. M.). La vaccination contre la fièvre jaune (1932–1936). [**Vaccination against Yellow Fever (1932–1936).**]—*Ibid.* pp. 1321–1324. [15 refs.]

viii. SOREL. La vaccination anti-amarile en Afrique Occidentale Française. Mise en application du procédé de vaccination Sellards-Laigret. [**Anti-Yellow Fever Vaccination in French West Africa. The Application of the Sellards-Laigret Method of Vaccination.**]—*Ibid.* pp. 1325–1356.

ix. STANTON (Thomas). Les insectes dans les aéroplanes au Kenya. [**Insects in Aeroplanes in Kenya.**]—*Ibid.* pp. 1357–1360. [See this *Bulletin*, 1936, Vol. 33, p. 343.]

x. BULLETIN DE L'OFFICE INTERNATIONAL D'HYGIÈNE PUBLIQUE. 1936. July. Vol. 28. No. 7. pp. 1361–1364.—Rapport de la commission de la fièvre jaune. (Session de mai 1936.) [**Report of the Yellow Fever Commission.**]

i. A useful summary of recent observations.

ii. During 1935 there were only 14 cases (all fatal) of yellow fever recorded from French West Africa, as compared with 23 the previous year ; the Ivory Coast remains the Colony most affected. A map is given showing the distribution of these cases which extend from Senegal to Dahomey.

Details are given of the clinical symptoms and autopsies of five of these cases, and the difficulties of diagnosis are well illustrated. The author recommends the systematic examination of the liver of any individual who succumbs to a rapid fever, no matter what the symptoms. Moreover it is desirable to examine the medulla, in addition to pieces of liver and kidney, in order to detect any possible changes in the nature

of the yellow fever virus, such as the development of neurotropic affinities.

iii. Details are given of the distribution of *Aëdes aegypti*, which is widely distributed throughout the Sudan, especially in the north and west where there are extensive epidemics of dengue. As a result of antimosquito measures they have now disappeared from Khartoum and Atbara, and almost so from Malakal, where only one breeding place was found out of 79,872 inspections. A suspected fatal case of yellow fever occurred at Malakal in January 1936, but the history and pathological changes were not sufficiently clear for a definite diagnosis to be made.

It is recommended that the principal aerodromes of the frontiers of the Sudan, Kassala, Geneina, Juba and Wadi Halfa, should be made "sanitary aerodromes," especially at Geneina.

Viscerotomy is now being practised in hospitals, and elsewhere when possible, on all undiagnosed fatal cases of fever dying in less than 9 days. Sera are being collected to see if anything comparable to jungle yellow fever occurs in the Sudan. Finally, each year the distribution of *Aëdes aegypti* is being determined.

iv. The author gives an historical account of recent yellow fever epidemics in Mexico up to 1922, and then the results of protection tests with sera collected from children and adults in these areas. The results indicate that yellow fever has been absent since 1925, but it is considered advisable to make a more extended series of tests in order to be certain of its exact distribution. Moreover, antilarval measures against mosquitoes should be intensified in regions where they are particularly abundant.

v. Details are given of the results of serum vaccinations in 107 Europeans, performed by Dr. STEFANOPOULO. No reaction attributable to the virus was ever observed, but serum reactions occurred in 7 of the cases, consisting of urticaria and joint pains lasting for 2 or 3 days.

vi. A further account of the technique used in the histological examination of specimens of liver, including a useful discussion of the interpretation of the appearances presented by different infections. [See this *Bulletin*, 1936, Vol. 33, p. 334.]

vii. A summary of the results of the vaccination of 951 persons against yellow fever by mixtures of virus and immune serum. In view of the possible danger of using a neurotropic virus a pantropic strain has been used recently and none of the 190 persons vaccinated with this virus has shown any very serious reactions. The pantropic strain is preserved in tissue culture, using a similar technique to that described by LLOYD, THEILER and RICCI [see this *Bulletin*, 1936, Vol. 33, p. 623], but employing as tissue chick embryos instead of mouse embryos, in view of the danger of introducing spontaneous mouse virus with the latter.

viii. Up to the end of 1935 a total of 23,890 vaccinations had been made in the French Colonies of West Africa, and 5,699 persons received three inoculations, using attenuated mouse virus without serum. The author first gives a detailed examination of the prophylactic value of vaccination and shows that the proportion of vaccinated persons is not sufficiently large to furnish any conclusive evidence. With regard to the reactions produced in man by the living virus, in 1934, 35·2 per cent. were found to give a reaction after the first inoculation, 27·1 per cent. after the second and 6·3 per cent. after the third. In 1935, there were 22·8 per cent. after the first, 14·8 after the second and 10·7 after the third. These reactions were found to fall into two groups.

The first, in which the symptoms developed about the 6th to 8th day after vaccination, includes the great majority of the cases. There is nothing of special interest about these reactions although they may be severe, but the patients invariably recover. The second group includes a number of cases in which reactions of the nervous system develop about the 12th to 15th day after vaccination. These cases are much more serious and it is necessary to reserve judgment as to their future history. Also their aetiology is uncertain, as they may be due either to yellow fever virus, or to a spontaneous mouse virus. An account of the clinical history of 20 of these patients is given in detail.

The author considers that although strong evidence of the efficacy of this method of vaccination has been brought forward, nevertheless the method must still be regarded as under discussion. Moreover, one cannot say that it is innocuous, not only for the few days after inoculation, but also after several months. It is very necessary, therefore, to follow up the history of any vaccinated subjects under various conditions, and it seems prudent not to think of making any systematic generalization of a method which still requires further study.

E. Hindle.

i. James (S. P.). Renseignements sur la fièvre jaune reçus au cours des six mois finissant le 30 septembre 1936. [**Information on Yellow Fever received during the Course of the Six Months ending 30th September, 1936.**]—*Bull. Office Internat. d'Hyg. Publique.* 1936. Dec. Vol. 28. No. 12. pp. 2329–2332.

ii. Sawyer (W. A.) & Bauer (J. H.). Résultats de l'enquête sur l'immunité amarile dans la région de la mer des Antilles. [**Results of an Inquiry into Yellow Fever Immunity in the Region of the Caribbean Sea.**]—*Ibid.* pp. 2333–2335.

iii. van Campenhout (Em.). Considérations relatives à la fièvre jaune au Congo Belge (épidémiologie, prophylaxie) d'après les renseignements extraits des récents Rapports. [**Observations concerning Yellow Fever in the Belgian Congo (Epidemiology, Prophylaxis) with Reference to Information in Recent Reports.**]—*Ibid.* pp. 2336–2339.

iv. Kirk (R.). Nouvelles recherches sur la fièvre jaune au Soudan Anglo-Egyptien. [**New Researches on Yellow Fever in the Anglo-Egyptian Sudan.**]—*Ibid.* pp. 2340–2345.

v. Bablet (J.). Sur le diagnostic différentiel entre la spirochétose ictéro-hémorragique et la fièvre jaune par l'examen histologique du foie. [**The Differential Diagnosis between Weil's Disease and Yellow Fever by Histological Examination of the Liver.**]—*Ibid.* pp. 2346–2352.

vi. Theiler (Max) & Smith (H. H.). L'emploi du sérum hyperimmun de singe dans la vaccination humaine contre la fièvre jaune. [**The Use of Monkey Hyper-immune Serum in Human Vaccination against Yellow Fever.**]—*Ibid.* pp. 2354–2357.]

vii. Bulletin de l'Office International d'Hygiène Publique. 1936. Dec. Vol. 28. No. 12. pp. 2358–2360.—Rapport de la commission de la fièvre jaune. (Session d'octobre 1936.) [**Report of the Yellow Fever Commission (October Session, 1936).**]

i. During the first 9 months of 1936, cases of yellow fever have occurred in Bolivia (16 cases), Brazil (179 cases) and Colombia (51 deaths, number of cases not stated). In Africa a total of 11 cases are

recorded from French West African Colonies, including Dahomey, Guinea, Ivory Coast, Niger Territory and Senegal, and 9 cases from British Colonies including the Sudan, Gold Coast and Nigeria.

Attention is called to the results of further mouse protection tests showing that the disease has been widespread in the Nuba mountains during the past 20 years, but clinically recognizable cases are rare. The examination of 76 monkeys from endemic areas showed that 15 contained specific antibodies against yellow fever, approximately the same percentage obtained by SOPER as a result of the examination of South American monkeys.

A Yellow Fever Research Institute has been established at Entebbe as a result of arrangements between the International Health Division of the Rockefeller Foundation and the Colonial Office in London.

In London 380 patients have now been vaccinated by the use of viscerotropic yellow fever virus attenuated by tissue culture, combined with hyper-immune serum, without any noticeable reactions.

ii. The authors have made mouse protection tests on 1,176 samples of serum collected from inhabitants of the islands of Barbados, Cuba, Jamaica, Porto Rico, St. Lucia and Trinidad. In addition specimens of serum from the mainland have also been examined including Mexico, Salvador, Guatemala, Honduras, British Honduras, Costa Rica and Nicaragua. With reference to the samples from the islands, 823 from subjects under 20 years old were all negative, an indication that the disease has not existed in these islands during the lives of the donors, but of the remaining 353 samples, 30 gave a positive protection test, the youngest of these being a Cuban aged 28 years.

The samples from the mainland, however, indicate that in Mexico the disease was very widespread previous to 1925, since when it has disappeared. Similar results were obtained in all the other countries examined with the exception of Costa Rica, where the disease seems to have been absent for the past twenty years.

iii. Attention is drawn to the fact that in the Lower Congo, the re-examination of the serum of natives giving a negative mouse-protective test in 1932 and 1933, has resulted in 6 per cent. now giving a positive test. Nevertheless, there has been no suspicion of the existence of yellow fever in this neighbourhood.

In the region of Libenge there has recently been an epidemic of infective jaundice. In 1933, before this epidemic, the examination of sera at one locality gave adults 12 per cent. positive, children all negative, and at a second locality 6 per cent. positive for all ages. A subsequent examination of sera of natives of these areas who gave no history of jaundice showed 29 per cent. positive and 9·4 per cent. doubtful, whilst of those recovered from jaundice 46·6 per cent. were positive, and 13 per cent. doubtful.

The special interest of these cases is that both Weil's Disease and yellow fever were excluded as possible causes of this epidemic of infective jaundice.

iv. During the past 18 months since January 1935, 3 sera out of 23 cases of jaundice have given positive mouse-protective tests, one from Juba, one from Malakal and the other from Wad Medani. But since 10 to 50 per cent. of the population may be positive these results are of doubtful significance in determining the nature of the jaundice.

The examination of 36 livers from cases of fever of obscure origin, fatal within 9 days, has given uniformly negative results.

The sera of 15 *Cercopithecus* monkeys have been tested and one gave a positive protection test. The results of mouse protection tests on sera collected from various districts of the Nuba mountains, gave positive results in every centre, ranging from 9·7 per cent. positive in Heiban up to 78·9 per cent. positive at Kau.

v. A general discussion and comparison of the histological changes observed in the liver in cases of yellow fever and Weil's Disease. The author advocates the further examination of the liver in cases of Weil's Disease in various parts of the world in order to exclude the possibility of any changes, resembling those in yellow fever, occurring under exceptional conditions. An appendix to the note contains a description by Bloch and Godin of the technique for the preparation of paraffin sections of the liver for the histological diagnosis of yellow fever. The pieces of liver are fixed in Duboscq-Brasil's *liquid for 24 hours, embedded in paraffin, sections cut 5 μ thick, and stained as follows:—

Mayer's haemalum 10 minutes; rinse in water; differentiate a few seconds in 90 per cent. alcohol containing 5 drops HCl per 100 ccm.; wash in tap-water for 5 minutes; stain for 3 minutes in 1 per cent. bluish Eosin (Microcolor) in tap-water; wash repeatedly in water; stain and differentiate for 3 minutes in an alcoholic solution of safranin; dehydrate very rapidly in absolute alcohol, which removes the excess of safranin, pass through toluol and mount in neutral Canada balsam.

vi. The hyper-immune serum is obtained by immunizing a rhesus monkey either by the injection of virus and immune serum or attenuated virus, and then after an interval of 6 or more weeks the animal is given a second injection of virulent viscerotropic virus. The serum is collected on the 9th day after this second injection and the serum from 10 or more animals is mixed together. This serum is found to have a titre at least 20 times, and may be 60 to 80 times, stronger than that used in ordinary vaccination. Consequently only about 4 cc. is all that is required for an average-sized person, instead of the large volume generally required for virus and immune serum vaccination. Hyperimmune serum and virus has now been used in the vaccination of 35 persons in New York, and one patient showed a post-vaccinial reaction which was severe for 6 days and slight pains in the knees persisted for some time afterwards. Such reactions seem to be rare, however, for 500 patients in Brazil were vaccinated by this method without any severe reactions being observed. *E. H.*

Paris: Office International d'Hygiène Publique. **Session of October, 1936. Report of the Yellow Fever Commission.** [Mimeographed translation. 2 pp.]

During the first nine months of 1936 the following cases of yellow fever have been notified; for South America, 16 in Bolivia, 181 in 7 States of Brazil, and 51 in Colombia; for West Africa, 13 cases in French Colonies and 7 in British Colonies. The results of mouse protection tests carried out in Central America and the islands of the Caribbean Sea agree in general with known epidemiological facts, but in the Anglo-Egyptian Sudan, a high proportion of positive tests, reaching 78 per cent. in the Kau district of Bahr-el-Ghazal, is not

* Picric Acid 1 gm.; Glacial Acetic Acid 10–15 ccm.; Formalin 50–60 ccm.; 75–80 per cent. Alcohol, 150 ccm.

correlated with the presence in the past of any disease clinically resembling yellow fever. In the Belgian Congo, the serum of persons negative in 1932 and 1933 has been re-examined and in 6 per cent. of these cases the serum had become positive although no disease resembling yellow fever had been known to occur in the meantime. An epidemic of infectious jaundice in the Libenge region, near Ubangi, was followed by a rise in the number of positive tests to 29 per cent. among natives who stated that they had not had jaundice and 46 per cent. among those who had recovered from jaundice. This outbreak, however, has not been identified with yellow fever [see iii above].

Viscerotropic yellow fever virus attenuated by culture has now been used, combined with immune serum, on 380 persons in London, 35 in New York and 500 in Rio de Janeiro, without producing any noticeable reaction attributable to the virus. Drs. SAWYER and BAUER have prepared a hyperimmune serum from the rhesus monkey with an average activity 20 times, and in some cases 60 to 80 times, the usual activity of human sera. Of 535 persons on whom this was used, only one showed a severe serum reaction. The immunity following vaccination evidently does not last as long as that following an attack of the disease, therefore it is advisable to re-examine the serum two to three years later and if necessary to re-vaccinate.

The Commission state as their opinion that a person exposed to yellow fever infection may be considered liable to introduce yellow fever into another country for a period of 6 days after leaving an infected area. *E. H.*

BEEUWKES (Henry). **Clinical Manifestations of Yellow Fever in the West African Native as observed during Four Extensive Epidemics of the Disease in the Gold Coast and Nigeria.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. June 30. Vol. 30. No. 1. pp. 61–86. With 3 charts.

The author gives an account of four epidemics of yellow fever in West Africa together with a description of the towns in which they occurred and facts bearing on the epidemiology.

The first of these epidemics, and also the first large outbreak of yellow fever exclusively among natives ever observed in West Africa, occurred during the spring and summer of 1926 at Asamankese, Gold Coast. It is estimated that the total number of cases was over 1,000, roughly 25 per cent. of the entire population, and the mortality was about 13 per cent. Severe as well as mild cases occurred among children, including two babes in arms. A second epidemic similar to the above occurred at Suhum, 42 miles north of Accra, immediately after the one at Asamankese. The percentage of cases affected seems to have been much lower, but exact estimates could not be made. The third epidemic occurred at Larteh, a town of about 4,000 inhabitants, 35 miles north-east of Accra, during 1927. It is estimated that the cases totalled over 200 and the deaths more than 30. The fourth epidemic included in this report occurred in 1928 at Ife, a primitive town of about 35,000 inhabitants, 55 miles due east of Ibadan. No accurate estimate could be made of the number of cases but protection tests carried out with the sera of two groups of children gave respectively 68 and 72 per cent. of positives.

Clinical observations were made on fatal, severe, and mild cases of yellow fever from these various centres and brief case histories are

given to illustrate the varying symptomatology. In 33 mild cases, the most constant symptoms were headache, pain in back and extremities, photophobia, anorexia, chill at onset, prostration, congestion of the eyes, typical tongue, small, coated, rather pointed, with red edges and tip. Icterus, vomiting and epigastric tenderness occurred in about half the cases and enlarged liver, tender liver, congested gums, bleeding gums, and vomiting with blood were present in diminishing frequency. Albuminuria was a constant feature. The temperature rose to 102·1°F. on the first day, accompanied by a pulse rate of 106, and the temperature returned to normal by the 5th day.

In 71 severe cases (not fatal) epigastric tenderness, vomiting, icterus, congested and bleeding gums, enlarged and tender liver, were among the symptoms showing higher percentages than in the mild cases ; and also casts were almost twice as common.

The paper should be consulted in the original for further details of the main clinical manifestations considered by the author. *E. H.*

SIERRA LEONE. ANNUAL REPORT OF THE MEDICAL AND SANITARY DEPARTMENT FOR THE YEAR 1935 [OAKLEY (Philip D.), Director of Medical Services]. Appendix G. pp. 78–81.—**A Health Report on the Incidence of One Definite and Several Suspected Cases of Yellow Fever in Freetown, Sierra Leone** [DUNCAN (J. A. A.), Assistant Director of Medical Services].

In spite of the many epidemics of yellow fever that have occurred along the West African coast, Freetown seemed to have remained uninfected since 1910, but in January 1935, the post-mortem findings in the case of a European resident showed that the disease was present, even if in a limited and sporadic form. Although no further cases occurred in Europeans, in February and March a series of cases arose in Africans suggestive of yellow fever, but only two out of 14 specimens of serum from these cases gave a positive mouse-protection test. On the occurrence of these two suspected cases Freetown was declared an infected area, but in the absence of any further cases at the end of March the port was declared free of infection. Nevertheless, since that date further cases showing similar signs and symptoms have occurred, but in no case has the patient died, nor has a positive result been obtained from the examination of the serum. *E. H.*

FINDLAY (G. M.) & DAVEY (T. H.). **Yellow Fever in the Gambia. II.—The 1934 Outbreak.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. July 31. Vol. 30. No. 2. pp. 151–164. With 2 figs. on 1 plate & 1 map.

A description of the epidemic of yellow fever that took place in Bathurst in 1934 during which, although only 6 cases were definitely diagnosed as yellow fever, conclusive evidence is brought forward that there were many more cases of the disease. Although yellow fever epidemics have never been described among Africans living in the Protectorate, a survey of the Gambia shows that in a number of villages from 20 to 33 per cent. of the inhabitants possess immune bodies to yellow fever.

In a discussion of this difficult problem the authors point out that there is no proof either that yellow fever is constantly present in

Bathurst or that it is introduced by shipping. The only external source of infection would seem to be the surrounding country where the possibility of the occurrence of jungle yellow fever cannot be ignored. However, the Bathurst outbreak was typically urban in character and the occurrence of an epidemic may be due to variation in one or more of the three factors concerned, *viz.*, the virus, *Aëdes aegypti*, and the non-immune human being.

The disease does not seem to be endemic in Bathurst but it is advisable to keep the mosquito index at zero in order to guard against the possibilities of reintroduction of the virus. *E. H.*

SOPER (Fred L.). **Jungle Yellow Fever. A New Epidemiological Entity in South America.**—Reprinted from *Rev. Hyg. e Saude Publica.* 1936. Apr. Vol. 10. No. 4. pp. 107–144. With 3 figs. on 2 plates, 4 graphs & 2 maps. [24 refs.]

A valuable summary of recent investigations on the epidemiology of yellow fever in South America with special reference to jungle yellow fever. The author includes details of observations on various outbreaks, from that in Espirito Santo, Brazil, in 1932, down to the one in Muchiri (Abapo), Bolivia, in May 1935.

The results of mouse protection tests with sera from monkeys captured in Colombia, Matto Grosso and Minas Geraes are given in the following table and show that many of these animals possess a naturally acquired immunity and support the view that they constitute a reservoir for the disease.

Results of Mouse Protection Tests with Sera from Monkeys captured in Colombia, Matto Grosso and Minas Geraes.

Captured in	Species	No. Exam.	No. Pos.
Restrepo, Intendencia de Meta, Colombia ...	*Callicebus ornatus* (1)	4	3
	Saimiri sciureus (1)	1	1
Planalto Region of Matto Grosso, Brazil :—			
Ponte Alta	*Pseudocebus apella* (L.) (2)	1	1
Deputado	*Pseudocebus apella* (L.) (2)	1	1
Furriel	*Pseudocebus apella* (L.) (2)	3	3
Minas Geraes, Brazil :—			
Mun. Araguary, (Vendinha)	*Hapale penicillata* (Goeffr.) (2)	2	0
Mun. Araguary, Faz. Patrona	*Pseudocebus apella* (L.) (2)	1	1
Mun. Campina Verde Faz. Rio Verde	*Pseudocebus apella* (L.) (2)	1	0
Mun. Patos, (Capellinha de Chumbo)	*Pseudocebus apella* (L.) (2)	1	0
Mun. Patos, Faz. Alberto ...	*Pseudocebus apella* (L.) (2)	1	0
Mun. Patos, Faz. Bananal ...	*Pseudocebus apella* (L.) (2)	57	8
Mun. Patos, Faz. Pantano ...	*Pseudocebus apella* (L.) (2)	20	0
	Total	93	18

(1) Identified in October 1935 by Mr. G. H. H. Tate, Assistant Curator of South American Mammals of the Department of Mammalogy of the American Museum of Natural History, New York.

(2) Identified by Professor Alipio de Miranda Ribeiro, Chefe da Secção de Zoologia, Museu Nacional, Rio de Janeiro, Brazil.

E. H.

MATHIS (Maurice). Diagnostic de la fièvre jaune par inoculation intracérébrale du sang de malade à la souris blanche. [**The Diagnosis of Yellow Fever by the Intracerebral Inoculation of the Patient's Blood into White Mice.**]—*C. R. Acad. Sci.* 1936. Sept. 14. Vol. 203. No. 11. pp. 547–548.

A description of the infection of 6 white mice by the intracerebral inoculation of the blood of a French patient in the neighbourhood of Dakar, who merely showed a very slight fever, and never any trace of albuminuria. A monkey also inoculated with the blood of this patient died of typical yellow fever. This is stated to be the first strain of mouse virus obtained direct from a human source. It is proposed to call it strain Ricou. *E. H.*

MATHIS (C.), DURIEUX (C.) & MATHIS (M.). La vaccination contre la fièvre jaune avec le vaccin au jaune d'oeuf de Laigret. [**Vaccination against Yellow Fever with Laigret's "Egg-Yolk Vaccine."**]—*Bull. Acad. Méd.* 1936. Oct. 20. 100th Year. 3rd Ser. Vol. 116. No. 31. pp. 226–238.

The authors state that using attenuated mouse virus in phosphatic suspensions from June 1934 to December 1935, 23,890 yellow fever vaccinations have been effected in French West Africa with only a single death [referred to below]. Recently the authors have used a phosphatic suspension of infected mouse brain mixed with egg yolk as recommended by NICOLLE and LAIGRET [this *Bulletin*, 1935, Vol. 32, p. 880].

Records are given of the results of vaccinating 450 persons, 400 whites and 50 negroes, at Dakar, by this method. The 50 negroes showed no reactions whatever ; the results with 376 of the whites are as follows :—no reaction 226, reaction after vaccination 150, including 67 mild, 49 moderate, and 34 prolonged reactions.

The mild reactions generally occur on the 5th or 6th day and consist merely of slight headache and a little malaise or lassitude. The moderate reactions generally last one to three days and the headache is rather more severe, accompanied by slight fever (37·5° to 39·5°C.).

The prolonged reactions are characterized by a relapse about the 18th day which may or may not be preceded by a primary vaccinial reaction. The symptoms observed are fever up to 40°C., headache, pain in the joints and muscles, photophobia, cutaneous hyperaesthesia, itching, stiffness of the neck, asthenia, etc. Sometimes gastric disturbances and hepatic insufficiency occur. Clinical details are given of representative cases, all of which recovered without any after effects.

The authors examined the blood of some of the vaccinated persons and by intracerebral inoculation into mice demonstrated the presence of yellow fever virus in the circulation, even in persons showing no reaction after vaccination. *E. H.*

BARRAUX (A.), MONTEL (E.) & BORDES (L. A.). Encéphalomyélite disséminée à forme subaiguë et vaccination antiamarile. [**A Subacute Form of Disseminated Encephalomyelitis and Anti-Yellow Fever Vaccination.**]—*Marseille-Méd.* 1936. June 5. Vol. 73. No. 16. pp. 755–759.

A discussion of the case of a patient who was vaccinated by Laigret's method in August 1934. He showed a violent reaction immediately

after the inoculation, but the symptoms disappeared after three weeks. Four months after the vaccination, however, the patient developed a disseminated encephalomyelitis to which he succumbed.

This case has been discussed previously and MOLLARET [this *Bulletin*, 1936, Vol. 33, pp. 619–20] was of the opinion that the symptoms were caused by a mouse virus ; whilst LAIGRET [*ibid.*, p. 620] thought that such accidents might be due to the neurotropic yellow fever virus. The present authors suggest the hypothesis of one of the known human viruses pre-existing in the patient and developing in the central nervous system, as a result of it becoming more susceptible after the yellow fever vaccination. *E. H.*

LAIGRET (J.). Au sujet des réactions nerveuses de la vaccination contre la fièvre jaune. [**Nervous Reactions after Vaccination against Yellow Fever.**]—*Bull. Soc. Path. Exot.* 1936. Oct. 14. Vol. 29. No. 8. pp. 823–827.

A reply to SOREL [see above, p. 337] concerning nervous reactions following yellow fever vaccination with attenuated mouse virus.

E. H.

LAIGRET (Jean) & DURAND (Roger). Virus isolé des souris et retrouvé chez l'homme au cours de la vaccination contre la fièvre jaune. [**A Virus isolated from Mice and recovered from Man in the Course of Vaccination against Yellow Fever.**]—*C. R. Acad. Sci.* 1936. July 20. Vol. 203. No. 3. pp. 282–284.

A description of the isolation of a virus from the brains of apparently normal mice by inoculation into guineapigs. The infection in the mice seems to be of very long duration but in guineapigs there is usually an incubation period of about 6 days followed by a febrile attack accompanied by marked emaciation also lasting for 6 days. About 40 per cent. of the guineapigs succumb to the infection and those that recover are immune against a second inoculation. Five monkeys were inoculated intracerebrally but only one showed an abnormal cerebrospinal fluid accompanied by fever.

This virus has been isolated from the cerebrospinal fluid of a man who had been vaccinated against yellow fever and showed a benign meningeal reaction. A suspension of fowl embryos, intended for tissue cultures, was inoculated into guineapigs and produced a transmissible infection apparently identical with the foregoing. It would seem, therefore, that the central nervous system of mice, man and fowl embryos may contain a neurotropic virus, which is pathogenic to guineapigs, but produces inapparent infections in rats and rabbits. The presence of this virus affords an explanation of some of the meningeal reactions following yellow fever vaccination by means of mouse virus. *E. H.*

STEFANOPOULO (G. J.), LAURENT (P.) & WASSERMANN (R.). Présence d'anticorps antiamarils dans le lait de femme immunisée contre la fièvre jaune. [**The Presence of Antibodies in the Milk of Women immunized against Yellow Fever.**]—*C. R. Soc. Biol.* 1936. Vol. 122. No. 23. pp. 915–917. [11 refs.]

The authors examined the milk of nine women ; one that had acquired immunity against yellow fever in nature, three that had been vaccinated by the serum-virus method, and five controls. The usual

protection tests were made in mice and it was found that the milk of the first four women all contained antibodies against yellow fever, whilst the five controls were negative.

The presence of these antibodies in the milk of immune women may be of interest in connexion with the probable immunity of new-born infants of such mothers. *E. H.*

FINDLAY (G. M.) & MACKENZIE (R. D.). **Attempts to produce Immunity against Yellow Fever with Killed Virus.**—*Jl. Path. & Bact.* 1936. July. Vol. 43. No. 1. pp. 205–208. [10 refs.]

The authors attempted to produce immunity in rhesus monkeys, hedgehogs and mice by the inoculation of large doses of yellow fever virus inactivated by means of formalin. These animals were inoculated with varying doses of the serum of a yellow fever monkey collected on the first or second day of fever and exposed to the action of 4 per cent. formol for 10 days at 4°C. The results are given in tabular form and show that with monkeys no immunity followed doses of 35 cc. inactivated serum. However, one of the hedgehogs was protected and 33 out of 50 mice survived when doses of 1 cc. were inoculated.

It would seem, therefore, that although dead yellow fever virus may produce immunity its use as a vaccine is impracticable owing to the very large amount of virus necessary to produce any effect. *E. H.*

FINDLAY (G. M.) & MAHAFFY (A. F.). **Paths of Infection of the Central Nervous System in Yellow Fever.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. Nov. 28. Vol. 30. No. 3. pp. 355–362. [25 refs.]

The authors studied the three possible routes of approach for yellow fever virus to the central nervous system. No evidence was obtained that the virus is able to travel along the peripheral nerves towards the central nervous system. Yellow fever virus can pass through the blood-brain barrier when this is artificially ruptured, and many other factors are well known to affect this barrier, but the authors consider that the method of approach from the naso-pharynx by the olfactory nerves is the most usual.

It is suggested that, as in certain other infections, the yellow fever virus may escape from the blood stream on to the nasal mucosa and thence pass by the olfactory nerves to the brain.

Experimental evidence in favour of this view is afforded by (1) finding virus on the nasal mucosa of a hedgehog, 24 hours after an intraperitoneal inoculation ; (2) the distribution of virus in the brains of young mice following intraperitoneal inoculation, showing that in the early stages there is a greater tendency for virus to be present in the fore-brain than in the mid- or hind-brain ; (3) the intranasal installation of picric acid in adult mice was found to prevent infection when the virus was instilled intranasally ; and (4) a similar intranasal instillation of picric acid into very young mice prevented infection when these were inoculated intraperitoneally with neurotropic yellow fever virus. *E. H.*

PENNA (H. A.). **The Production of Encephalitis in *Macacus rhesus* with Viscerotropic Yellow Fever Virus.**—*Amer. Jl. Trop. Med.* 1936. May. Vol. 16. No. 3. pp. 331–339.

By the intraperitoneal inoculation of yellow fever immune serum followed immediately by the intracerebral inoculation of viscerotropic

yellow fever virus into *Macacus rhesus*, the author was able to produce encephalitis in these monkeys without any visceral changes developing. Serial intracerebral subinoculations with this virus, using the same technique, was carried out in two series of monkeys, in one of which a modification of the virus was noted in the 35th passage, when it acquired neurotropic affinities. In the other series the virus at the 40th passage still produced visceral lesions unless the intracerebral inoculation was accompanied by the injection of immune serum.

The first series was then carried on by intracerebral inoculations without immune serum and up to the 8th passage (48th in total series) all the monkeys developed encephalitis without liver lesions. Of three monkeys inoculated in the 9th passage, one developed encephalitis without liver lesions; the second, both encephalitis and necrotic changes in the liver; and the third monkey died in 4 days with typical yellow fever lesions in the liver and no signs of encephalitis. The series was carried on by intracerebral inoculations to the 85th passage by the use of immune serum and when again tested in 7 monkeys without immune serum all died of encephalitis. The changes obtained seem to be sufficiently marked to justify the name of neurotropic, but the author does not believe that it is entirely comparable to the mouse-brain-adapted virus of the same number of passages.

The encephalitis due to inoculation with viscerotropic yellow fever virus was not found to differ clinically or pathologically from the encephalitis produced in monkeys by inoculation with "mouse virus."

E. H.

LYNCH (Clara J.) & HUGHES (Thomas P.). **The Inheritance of Susceptibility to Yellow Fever Encephalitis in Mice.**—Reprinted from *Genetics*. 1936. Mar. Vol. 21. pp. 104–112.

SAWYER and LLOYD [see this *Bulletin*, 1932, Vol. 29, p. 198] noticed that different strains of mice showed variations in their susceptibility to intracerebral inoculation of yellow fever virus and the present authors have investigated the inheritance of this susceptibility. Mice from two sources were found to give different mortality rates varying by 31·2 per cent. When these strains were crossed the hybrids showed a mortality less than that of the susceptible strain of mice. By crossing the hybrid back to the susceptible strain the mortality rate was increased, and by crossing back to a more resistant strain the rate was lowered.

Offspring from two susceptible parents were more susceptible than the offspring from one or two resistant parents.

Susceptibility did not seem to be modified by sex. As a result of these experiments it is concluded that hereditary factors for resistance to yellow fever encephalitis are present in mice. *E. H.*

MATHIS (M.). Sensibilité de la souris grise Dakaroise au virus amaril (32 passages en série). [**The Susceptibility of the Dakar Grey Mouse to Yellow Fever Virus (32 Passages in Series).**]—*Bull. Soc. Path. Exot.* 1936. July 8. Vol. 29. No. 7. pp. 703–707.

The Dakar variety of wild mouse, *Mus musculus* sub-sp. *gentilis* and *spretus* Braut, was found to be refractory against infection with viscerotropic yellow fever virus as tested by intracerebral inoculations

into 23 animals. On the other hand this species is susceptible to the neurotropic virus and 32 passages in series were effected without any appreciable change being produced in the virulence of the strain.

E. H.

ROY (D. N.). **On the Role of Blood in Ovulation in** *Aëdes aegypti*, **Linn.**—*Bull. Entom. Res.* 1936. Sept. Vol. 27. Pt. 3. pp. 423–429. With 1 fig.

The author fed *Aëdes aegypti* on a human volunteer, and in some cases interrupted the feeding at various stages in the process whilst others were allowed to feed to repletion. The weight of blood ingested was then determined and the number of eggs subsequently laid by each group of mosquitoes to determine whether the blood had acted simply as a physico-chemical stimulus to the ovarian follicles or provided nutrient material for their development.

The results indicate that there is a quantitative relationship between the weight of the blood meal and the number of eggs produced. Nevertheless, this relationship does not seem to be on a graded quantitative scale, and the author finds evidence to support the view that two factors are involved, one acting directly on the follicles, stimulating them to activity, the other providing actual material for the formation of the eggs.

No evidence was obtained in support of the view that the number of eggs deposited by a mosquito varies directly with its size and it is likely that the amount of blood in the stomach exercises a greater influence. *E. H.*

MERRETT (W. E. Stanley). A Brief Review of Recent Trends in Yellow Fever Research.—*West African Med. Jl.* 1936. Oct. Vol. 9. No. 1. pp. 2–9. [38 refs.]

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

CAMINOPETROS (Jean) & TRIANTAPHYLLOPOULOS (E.). Existence en Grèce d'une fièvre récurrente dont le spirochète revêt les caractères de "*Spirochaeta hispanica*" agent de la fièvre récurrente hispano-africaine. [**The Existence in Greece of a Relapsing Fever of which the Spirochaete recalls the Characters of** *Spirochaeta hispanica*, **the Causative Organism of Spanish-African Relapsing Fever.**]—*Bull. Acad. Méd.* 1936. June 16. 100th Year. 3rd Ser. Vol. 115. No. 23. pp. 822–825. Also in *Ann. Parasit. Humaine et Comparée.* 1936. Sept. 1. Vol. 14. No. 5. pp. 429–432.

Cases of relapsing fever of unknown origin have been recorded from several villages in the plains of Messina, Peloponnesia, but hitherto the nature of this fever has not been determined. The authors have inoculated the brains of wild rats caught in these regions into guinea-pigs, and isolated a spirochaete which in its general character, including transmission by *Ornithodorus erraticus*, resembles *Spirochaeta hispanica.* Cross-immunity experiments were made with the Moroccan strain and the Greek strain would seem to be a variety of the Spanish-Moroccan strain, and the name of *S. hispanica* var. *peloponesica* is proposed for it. A number of *Rhipicephalus sanguineus* collected from a dog suffering from the disease were inoculated into 5 guineapigs, one of which became infected with this spirochaete. *E. Hindle.*

CACCIAPUOTI (Raffaele). Febbre ricorrente nell' Acchelè Guzai (Eritrea). [**Relapsing Fever in the Acchelè Guzai (Eritrea).**]—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1936. May. Vol. 17. No. 5. pp. 289–301.

The author has himself observed 40 cases and 20 others in the locality were reported to him as occurring among a battalion stationed in Addi Caieh. The first four of the last all died; the outbreak took place at the end of August 1935. In September in a nearby village there were 4 more cases, 1 fatal; in November in the same district of Scimezana, he saw 20 cases in 4 houses, three of the patients died. In two other villages of the same district 3 died out of 13 attacked, and one of three seen in Addi Uirà. Among the sixty there were twelve deaths. In 33 of the 40 patients under the author's care diagnosis was made by finding the spirochaete in the blood. Brief details of all 40 are given, followed by an analysis of individual symptoms as regards their presence and frequency. *H. H. S.*

CACCIAPUOTI (Raffaele). Contributo allo studio della febbre ricorrente da pidocchi in Eritrea. [**Louse-borne Relapsing Fever in Eritrea.**]—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1936. Sept. Vol. 17. No. 9. pp. 546–556. With 1 map.

The author examined inhabitants in 36 villages scattered in 11 districts in Acchelè Guzai (Eritrea). The numbers of inhabitants in a village ranged from 100 to 700, and the total populations of all the districts was 10,550. Among them were 219 found suffering from relapsing fever and 29 died, a fatality rate of 13·2 per cent. A brief note is made of the chief clinical symptoms and their relative prevalence. *H. H. S.*

BALTAZARD (M.). Individualité stricte des souches marocaines du spirochète hispano-africain. [**The Strict Individuality of Moroccan Strains of Spanish-African Relapsing Fever.**]—*Bull. Soc. Path. Exot.* 1936. June 10. Vol. 29. No. 6. pp. 667–671.

The author has made cross-immunity tests with 12 strains of *Spirochaeta hispanica*, seven isolated from wild rats in Casablanca, two from *Ornithodorus*, and three from human cases of relapsing fever, also in Casablanca. Details are given showing that infection with each of these strains in guineapigs and rats was followed by immunity only against that particular strain, and that reinoculation successively with any or all of the other strains was followed by infection.

These observations confirm those of NICOLLE and his collaborators in Tunis, who have never found any two strains of relapsing fever which were antigenically the same. *E. H.*

ACKERMANN (Victor) & PROTASOV (Nikolai). Einige klinische und parasitologische Beobachtungen beim experimentellen Zecken-Rückfallfieber. [**Some Clinical and Parasitological Notes on Experimental Tick Fever.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Aug. Vol. 40. No. 8. pp. 352–358. [14 refs.]

The authors have studied the Central Asiatic strain of tick fever in guineapigs and find that two types of movement can be distinguished in the spirochaetes, one serpentine and the other rotatory, depending on the external conditions. A ring-like modification is stated to be a protective modification.

Spirochaetes were found to retain their motility and virulence in blood kept in the ice-chest up to 107 days. They multiplied the first 2 to 4 days and then their numbers gradually diminished. Hydrogen peroxide had very little effect on the organisms. Neosalvarsan (1 : 1,000) killed the spirochaetes and quinine (1 : 1,000) had an even stronger lethal action.

The peripheral blood of infected guineapigs was found to contain spirochaetes within 24 hours after inoculation. The first attack of relapsing fever in guineapigs is not followed by any lasting immunity, but after repeated attacks the immunity is probably more persistent.

The spirochaetes were found to pass through the placenta and infect the unborn young. *E. H.*

BRUMPT (E.). Sur l'identification des spirochètes récurrents. Etude d'une souche de *Spirochaeta recurrentis* (?) conservée depuis longtemps sur souris, dans divers laboratoires d'Allemagne. [**The Identification of Relapsing Fever Spirochaetes. The Study of a Strain of** *Spirochaeta recurrentis* (?) **preserved for Long Periods in Mice, in Various German Laboratories.**]—*Ann. Parasit. Humaine et Comparée.* 1936. Nov. 1. Vol. 14. No. 6. pp. 586–596. [25 refs.]

An interesting discussion of the nature of the Frankfort strain of *Spirochaeta recurrentis*, generally supposed to be of Russian origin, which after thousands of passages in mice has lost its pathogenicity to man, and has been used for some years in pyretotherapy.

This strain differs from four Chinese strains of *S. recurrentis* studied by the author, in its power of surviving for at least 27 months in the body of *Ornithodorus moubata*, in which, however, it does not invade either the salivary glands or the coxal fluid. On the other hand, the Frankfort strain disappears in a few weeks from the body of *Ornithodorus tholozani*, the natural carrier of *S. persica*. This spirochaete will live for at least 18 months in *O. moubata* and for long periods in *O. talajae*, but neither of these ticks shows infection of the salivary glands or coxal fluid.

Similarly *S. turicatae* retains its virulence for at least 19 months in *O. moubata*, and 14 months in *O. migonei*, but neither of these ticks can transmit the infection by the bite. *Spirochaeta novyi*, which is probably a race of *S. recurrentis*, because it persists for at least 9 days in the louse, lives only for a few days in *O. moubata* and *O. turicata*.

In view of the long survival of the Frankfort strain in *O. moubata*, the author considers that it is probably a strain of *S. duttoni*, which after thousands of passages in mice has lost its power of invading the salivary and coxal glands, and in consequence is not transmitted by the bite of ticks containing the spirochaete. *E. H.*

CHUNG (Huei-lan). **Studies on the Transmission of Relapsing Fever in North China. I. Preliminary Observations.**—*Chinese Med. Jl.* 1936. Dec. Vol. 50. No. 12. pp. 1723–1734. With 4 figs. on 2 plates.

The author made some observations on an outbreak of relapsing fever at an orphanage in Peiping. Nine out of twelve body-lice from the garments of patients were found to contain mobile spirochaetes, and splenectomized squirrels inoculated with the contents of other lice from the same source became infected with the disease. Bed-bugs fed on infected squirrels contained living spirochaetes for at least 25½ hours, and these organisms produced infection in normal splenectomized squirrels by instillation in the conjunctiva and oral cavity. Squirrel-lice from experimentally infected Chinese squirrels also contained spirochaetes which were similarly shown to be infective. *E. H.*

CHUNG (Huei-Lan) & FENG (Lan-Chou). **Studies on the Development of *Spirochaeta recurrentis* in Body Louse. A Preliminary Report.**—*Chinese Med. Jl.* 1936. Sept. Vol. 50. No. 9. pp. 1181–1184.

The authors fed different batches of body lice, bred in the laboratory, on a [presumably Chinese] relapsing fever patient whose blood contained 20–30 spirochaetes per oil immersion darkfield. They were subsequently fed on normal individuals and dissections made every day until all the lice were dissected. The darkground method of examination was used throughout, supplemented by inoculating the suspected material into splenectomized squirrels.

The gastric juice was found to be detrimental to these spirochaetes and none was present in the stomach 8 hours after an infective feed. Only about 1 to 5 per cent. gain access into the coelomic fluid and tissues where they multiply. Spirochaetes can be found in the coelomic fluid and legs within 2 hours and remain constantly present in an infective form for at least 18 days. They multiply in this position

and there is no necessity nor reason for accepting the theory of invisible forms being present.

The faeces of infected lice are not infectious although dead spirochaetes may be found in them during the first 6 hours after an infective feed. Moreover, the salivary glands and Malpighian tubules do not contain *S. recurrentis*. Congenital transmission of the infection was not observed and conjugation does not transmit the spirochaete from lice of one sex to those of the opposite sex. *E. H.*

FENG (Lan-Chou) & CHUNG (Huei-Lan). **Studies on the Development of** *Spirochaeta duttoni* **in** *Ornithodorus moubata.* **A Preliminary Report.**—*Chinese Med. Jl.* 1936. Sept. Vol. 50. No. 9. pp. 1185–1190.

Using similar methods to those outlined in the preceding article, the authors have studied the development of a French Congo strain of *S. duttoni* in *Ornithodorus moubata.* After feeding on an infected animal the ticks were kept at 25° to 30°C. and dissected at various intervals up to 41 days after the infective meal.

Spirochaetes were found in the stomach up to the 11th day but from the 12th day onward no more were seen there. Within 6 hours after feeding spirochaetes appear in the legs and coelomic fluid, from which they invade the salivary glands, nerve ganglion, and the coxal glands and their reservoirs. Multiplication by transverse division takes place in these organs as well as in the body cavity and after the 3rd or 4th day numerous spirochaetes are present. Mice inoculated with organs containing spirochaetes always became infected, while those injected with the Malpighian tubules and faeces in which spirochaetes could not be found remained sterile.

From these experiments the authors conclude that it is unnecessary to assume the presence of a granular phase in the life history of *Spirochaeta duttoni* in the tick. *E. H.*

DE BUEN (Sadi). Observaciones sobre el comportamiento del "Treponema hispanicum" en el "Ornithodorus erraticus." II. Sobre la teoría de la fases "letal" y "normal" del parásito de la recurrente española. [**On the Behaviour of** *Spirochaeta hispanica* **in** *Ornithodorus erraticus.*]—*Rev. San. e Hig. Pública.* 1936. July. Vol. 11. No. 7. pp. 13–18.

Previous investigations led the author to state an hypothesis that there existed a phase of the virus which caused a high rate of deaths in mice, a phase in the life of the spirochaete passed in the stomach of the tick, and another phase, present in the salivary glands of the tick, which set up the more "normal" type of disease in mice. Further research has caused him to modify this view. He found that from 5 to 21 days after the infecting feed the "virus" is visible in the stomach, but this when injected gives rise to the normal disease. Later, when there is salivary gland infection, it is not possible to determine with certainty whether the infection is transmitted by the latter, or by regurgitation from the stomach. The author states: "Fresh experiments do not confirm the hypothesis that there are two phases—a lethal and a normal—in the life of the parasite in the tick."

H. H. S.

POPOW (P. P.) & ACHUNDOW (I.). Das Vorkommen des Ornithodorus Lahorensis Neumann, 1908 in Aserbajdjan und die Frage ueber die Anwesenheit des Zeckenrückfallfiebers in A.S.S.R. [**The Occurrence of** *Ornithodorus lahorensis* **Neumann, 1908 in Azerbaijan and the Problem of the Presence of Tick-transmitted Relapsing Fever in A.S.S.R.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. July. Vol. 40. No. 7. pp. 289–295. With 4 figs. [28 refs.]

Ornithodorus lahorensis was found to occur in Azerbaijan in considerable numbers, favourite localities for them being crevices in the stone walls of the old caravanseries and especially cracks in the wood of the sheep stalls. In addition the burrows of rodents are considered to be another probable site.

Details are given of a spontaneous case of typical relapsing fever, following the bite of an undetermined species of tick. *E. H.*

BRUMPT (E.). Non transmission de la fièvre récurrente de l'Asie centrale à *Spirochaeta persica*, par l'*Ornithodorus canestrinii*. [**The Non-Transmission of the Relapsing Fever of Central Asia** (*Spirochaeta persica*), **by** *Ornithodorus canestrinii*.]—*Ann. Parasit. Humaine et Comparée.* 1936. Sept. 1. Vol. 14. No. 5. pp. 433–435.

Two specimens of *Ornithodorus canestrinii* were fed on a guineapig infected with *Spirochaeta persica* and showing about 20 spirochaetes per field. These two ticks after intervals of 3 months and a year were fed on normal guineapigs, neither of which became infected.

E. H.

BRUMPT (E.). Action nulle du froid sur le pouvoir infectieux des Argasinés vecteurs de fièvres récurrentes. [**The Absence of any Effect of Cold on the Infective Power of Argasid Carriers of Relapsing Fever.**]—*Ann. Parasit. Humaine et Comparée.* 1936. Sept. 1. Vol. 14. No. 5. pp. 436–439.

Respective batches of *Argas persicus* infected with fowl spirochaetosis, *Ornithodorus erraticus* infected with *Spirochaeta hispanica*, and *O. tholozani* infected with the relapsing fever of Central Asia, were kept in the ice chest at 5° to 7°C. for several weeks and then fed on susceptible hosts. All the animals bitten by these ticks were infected as readily as control animals on which ticks fed that had not been exposed to the action of cold. *E. H.*

BRUMPT (E.). Transmission expérimentale exceptionnelle de la fièvre récurrente du Maroc à *Spirochaeta hispanica* par la tique cosmopolite *Rhipicephalus sanguineus*. [**The Exceptional Experimental Transmission of Moroccan Relapsing Fever** (*S. hispanica*) **by the Cosmopolitan Tick** *R. sanguineus*.]—*Ann. Parasit. Humaine et Comparée.* 1936. Nov. 1. Vol. 14. No. 6. pp. 564–570. [22 refs.]

About 3,500 newly hatched hexapod larvae of *Rhipicephalus sanguineus* were allowed to become engorged on a guineapig infected with *Spirochaeta hispanica*. Twenty-seven days later 800 nymphs hatched from these larvae were fed on a guineapig, which showed

spirochaetes in its blood after an incubation period of 9 days. A second guineapig inoculated 2 days later with a suspension of the contents of 60 of these nymphs remained uninfected. In another similar experiment, one out of three guineapigs became infected, but of a total of 11 guineapigs, either bitten or inoculated with the contents of these ticks, only these two became infected, and attempts to infect a young dog were also negative.

It would seem, therefore, that *Rhipicephalus sanguineus* is of little importance as a carrier of *S. hispanica.* *E. H.*

BRUMPT (E.). L'ixodiné *Rhipicephalus sanguineus* ne transmet pas expérimentalement la fièvre récurrente de l'Asie Centrale à *Spirochaeta persica.* [**The Ixodid** *R. sanguineus*, **experimentally does not transmit Central Asiatic Relapsing Fever** (*S. persica*).]—*Ann. Parasit. Humaine et Comparée.* 1936. Nov. 1. Vol. 14. No. 6. pp. 571–573.

Large numbers of larval and nymphal stages of *R. sanguineus* were fed on guineapigs infected with *Spirochaeta persica*, and subsequently fed on, or their contents inoculated into, normal guineapigs, with uniformly negative results. *E. H.*

BRUMPT & CAMINOPETROS (Jean). Non transmission de la fièvre récurrente grecque à *Spirochaeta hispanica* var. *peloponesica*, par la tique *Rhipicephalus sanguineus.* [**The Non-Transmission of Greek Relapsing Fever** (*S. hispanica* **var.** *peloponesica*) **by the Tick** *R. sanguineus.*]—*Ann. Parasit. Humaine et Comparée.* 1936. Nov. 1. Vol. 14. No. 6. pp. 574–577.

A record of negative attempts to infect 36 guineapigs by the bites or inoculation of the contents of *R. sanguineus* that had previously fed on animals infected with the Greek strain of *S. hispanica.*

E. H.

BRUMPT (E.). Le spirochète (*Spirochaeta recurrentis*) de la fièvre récurrente à poux de Chine, n'est pas transmis expérimentalement par la piqûre de l'*Ornithodorus moubata* et ne se conserve pas chez cet acarien. [**The Spirochaete of Chinese Relapsing Fever** (*S. recurrentis*) **is not Transmitted Experimentally by the Bite of** *Ornithodorus moubata* **and does not persist in that Tick.**]—*Ann. Parasit. Humaine et Comparée.* 1936. Nov. 1. Vol. 14. No. 6. pp. 578–585. [21 refs.]

A record of negative attempts to transmit two strains of *Spirochaeta recurrentis* by the bites or inoculation of the contents of *Ornithodorus moubata.* Dr. Feng Lan-Chou, in Peking, found that these spirochaetes persisted not longer than a week in *O. moubata.* *E. H.*

BRUMPT (E.). Distribution géographique et rôle en pathologie humaine de l'*Ornithodorus savignyi.* [**The Geographical Distribution and Significance in Human Pathology of** *Ornithodorus savignyi.*]—*Ann. Parasit. Humaine et Comparée.* 1936. Nov. 1. Vol. 14. No. 6. pp. 640–646. [28 refs.]

This species has been found by T. MONOD in large numbers in the neighbourhood of Azaouad, Timbuctoo, and is widely distributed

throughout Africa and various parts of Asia, including Ceylon (CRAWFORD). Nevertheless there is no record of *O. savignyi* ever being naturally infected with any strain of spirochaete, although experimentally it can transmit by bite several species, including *Spirochaeta duttoni*, *S. hispanica*, and *S. normandi*. The fact that in regions where *O. moubata* is infected with *S. duttoni*, and *O. savignyi*, living under the same conditions and having similar habits, is uninfected, may be explained by the fact that in the latter the spirochaetal infection does not seem to be transmitted hereditarily, which diminishes the chance of any natural infection becoming established in it. *E. H.*

HERMS (W. B.) & WHEELER (C. M.). *Ornithodorus hermsi* **Wheeler as a Vector of Relapsing Fever in California.**—*Jl. Parasitology.* 1936. June. Vol. 22. No. 3. pp. 276–282.

Since the first two cases of relapsing fever recorded in California in 1922 [see this *Bulletin*, 1923, Vol. 20, p. 132] a total of 95 cases had been recorded, 46 of which occurred at Big Bear Lake and 26 at Lake Tahoe, and all at elevations of 5,000 to 8,000 ft.

Infected *Ornithodorus hermsi* have been found in the nests of rodents (chipmunks, etc.) at both these localities, and hereditary transmission of the spirochaetes from the female tick to the egg and resulting larva has been effected for both strains. Infections can be produced in mice by the bites of infected ticks at all stages and spirochaetes usually appear in the blood after about five days' incubation. Once infected a tick remains infective for the remainder of its life.

The authors include a number of observations on the life-history and habits of this tick, which is primarily a parasite of rodents but will readily feed on other animals and man. The cycle from egg to egg requires about 4 months in the case of ticks kept in the laboratory at 75°F. *E. H.*

DAVIS (Gordon E.). *Ornithodoros turicata*: **the Possible Vector of Relapsing Fever in Southwestern Kansas. Preliminary Report.**—*Public Health Rep.* 1936. Dec. 11. Vol. 51. No. 50. p. 1719.

Eleven cases of relapsing fever were reported from Clarke County, Kansas, by Dr. H. O. CLOSSON * in 1934 and other cases have been reported subsequently from this and adjoining counties.

The author has recently collected approximately 2,000 specimens of *Ornithodorus turicata* in Clarke County, from rodent burrows and attached to various animals, including rodents, prairie-dogs, owls and terrapins, and from one sand-hole containing 11 terrapins (*Terrapene ornata*) no less than 1,197 ticks were removed. The ticks were tested for infectivity by feeding on white rats, and three strains of spirochaetes were recovered from three localities, one of which was a ranch where a case of relapsing fever had occurred. It seems reasonable to assume, therefore, that *O. turicata* may be implicated in the transmission of relapsing fever in this area. *E. H.*

CERCIELLO (Raffaele). Considerazioni cliniche su alcuni casi di febbre ricorrente osservati in Senafè (Eritrea).—*Giorn. Ital. di Malat. Esot. e Trop.* 1936. Nov. 30. Vol. 9. No. 11. pp. 241–4, 247–50, 253, 255–6. [10 refs.]

* 1934. *Journal of the Kansas Medical Society*, Vol. 35, No. 2.

ECKHARDT (A. E.) & ECKHARDT (G.). Behandlung zerebraler Erscheinungen bei Rekurrens mit Fiebertherapie. (Vorläufige Mitteilung.) [**The Treatment of Cerebral Symptoms in Relapsing Fever by Means of Fever Therapy. (Preliminary Note.)**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. July. Vol. 40. No. 7. pp. 301–303.

The description of a case of relapsing fever in which large doses of neosalvarsan did not prevent the development of severe cerebral symptoms. The patient's temperature was 37·6°C. and no spirochaetes were found in the blood. On the analogy of the treatment of syphilis the authors gave injections of T.A.B. intravenously, followed by doses of neosalvarsan and found that the cerebral symptoms disappeared.

E. H.

SAUTEREY (Pierre). Les idées modernes sur les fièvres récurrentes. [**Modern Views on Relapsing Fever.**] [Thesis presented to the Faculty of Medicine, Algiers.]—108 pp. [Bibliography.] Imp. F. Michaud.

An incomplete summary of the literature dealing with recent observations on relapsing fever, and notes on the history of the disease containing nothing original. *E. H.*

See also p. 120, RUSSELL, **Observations on Immunity in Relapsing Fever and Trypanosomiasis.**

LEPTOSPIROSIS.

HOME OFFICE. **Departmental Committee on Compensation for Industrial Diseases. Third Report to the Right Honourable the Secretary of State for the Home Department by the Departmental Committee appointed to inquire and report as to Certain Proposed Extensions of the Schedule of Industrial Diseases to which Section 43 of the Workmen's Compensation Act, 1935, applies.** [ROLLESTON (Humphry), Chairman].—16 pp. [46 refs.] 1936. London: H.M.S.O. [4*d.*]

This report includes a general account of the main features of infection with *Spirochaeta icterohaemorrhagiae*, discussed especially with regard to methods of diagnosis and whether it should be scheduled as an industrial disease under Section 43 of the Workmen's Compensation Act, 1915. From 1924 to October 1935, 424 notifications of the disease were received by the Local Authorities in Scotland, but of these cases only 77 were definitely accepted cases, 23 of which were fatal. The occupations of these 77 cases were 25 miners, 38 fishworkers (mainly in Aberdeen during 1934 and 1935), 6 agricultural workers and 8 miscellaneous.

After reviewing the evidence the Committee recommends that infection by *S. icterohaemorrhagiae* should entitle a workman to compensation for disablement but only if confirmed by bacteriological or serological examination. In fatal cases pathological evidence of the infection should be accepted.

In the event of the disease becoming more widespread or of other developments, it may be found that it ought no longer to be scheduled as an industrial disease. *E. Hindle.*

GRAF (H.) Ueber einen Fall von Weilscher Krankheit in Kamerun. [**A Case of Weil's Disease in the Cameroons.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Oct. Vol. 40. No. 10. pp. 456–460. With 2 figs.

The description of a typical case in a European who probably acquired the infection from a swimming pool. Leptospirae were found in the urine and when inoculated into guineapigs produced typical and fatal infections. In addition serological tests with the patient's blood furnished additional confirmation of the nature of the infection.

E. H.

ZIMMERMANN (E.). Ueber ein verbessertes Kulturverfahren der *Spirochaeta icterogenes.* [**An Improved Culture Medium for** *Spirochaeta icterogenes.* (? *S. icterohaemorrhagiae*).]—*Zent. f. Bakt.* I. Abt. Orig. 1936. Sept. 10. Vol. 137. No. 5. pp. 280–282.

The culture of Weil's spirochaete rarely presents much difficulty, once it has become established, but occasionally primary cultures do not succeed. The author finds that the addition of one or two loopfuls of a sterile culture of yeast to about 1·0 cc. of their ordinary medium (10 per cent. rabbit serum in tapwater) greatly improves the growth of spirochaetes. This improvement continues in subcultures not containing yeast cells. This favourable action of yeast is destroyed by heating to 100°C. for 5 to 10 minutes and also when the cells are removed by centrifuging. *E. H.*

MURGATROYD (Frederick). **Chronic Meningitis in Weil's Disease.**—*Brit. Med. Jl.* 1937. Jan. 2. pp. 7–11. [12 refs.]

A description of a prolonged case of Weil's disease associated with a progressive type of meningitis in a farm labourer. When first seen, about two weeks after the beginning of fever, the patient was jaundiced and S. *icterohaemorrhagiae* was found in the urine, but a week later the patient's condition had improved and the jaundice had almost disappeared. About a month later the fever returned, and four months after the beginning of the illness meningeal symptoms developed, and the patient's condition got steadily worse until anti-leptospiral serum was administered. Leptospira were found in the cerebrospinal fluid and urine up to 25 and 33 weeks respectively from the onset of the disease, the diagnosis being made by means of guineapig inoculation.

In spite of the long duration of this infection both the cerebrospinal fluid and blood serum possessed practically no agglutinating power against the infecting organism and against various other strains of leptospira.

The author concludes with a useful discussion of the meningitic manifestations of Weil's disease, and points out the necessity for considering the possibility of this infection in any obscure case of meningitis, or even in cases of obscure pyrexia. *E. H.*

MURRAY (R. Elliott) & FIELDING (John W.). **Notes on the Silver Impregnation of** *Leptospira icterohaemorrhagiae.*—*Med. Jl. Australia.* 1936. May 2. 23rd Year. Vol. 1. No. 18. pp. 610–611. With 2 figs. on 1 plate.

The authors have studied various methods of silver impregnation for leptospira, and find that alkaline fixatives have a destructive influence, consequently tap water should never be used in diluting formalin or washing tissues as it is frequently alkaline.

By raising the temperature the impregnation can be completed in 5 hours using the following technique :—

" 1. Cut strips of tissue 1·5 millimetres thick.
" 2. Fix one hour at 50°C. or 18 hours at room temperature in (*a*) F.A.A.* or (*b*) F.A.S.†
" 3. 70 per cent. alcohol, 30 minutes at 50°C.
" 4. 1 per cent. silver nitrate, 30 minutes at 50°C.
" 5. Wash in five to six changes of distilled water.
" 6. Develop 60 minutes at 50°C. in (*a*) 1 per cent. pyrogallic acid in 5 per cent. formalin, (*b*) 1 per cent. pyrogallic acid, or (*c*) 1 per cent. quinol.
" 7. Wash in five to six changes of distilled water.
" 8. 50 per cent. alcohol, 15 minutes at 50°C.
" 9. 70 per cent. alcohol, 15 minutes at 50°C.
" 10. 90 per cent. alcohol, 15 minutes at 50°C.
" 11. Absolute alcohol, 15 minutes at 50°C.
" 12. Repeat absolute alcohol, 15 minutes at 50°C.
" 13. Xylol, 15 minutes at 50°C.
" 14. 46° to 48°C. melting point paraffin, 15 minutes.
" 15. 50° to 52°C. melting point paraffin, 15 minutes.
" 16. Embed in a suitable paraffin."

Microphotographs are reproduced illustrating the deleterious action of an alkaline fixative on the staining reactions of leptospira in the liver of an infected guineapig. *E. H.*

POT (A. W.). **A Macroscopic Agglutination Test in Weil's Disease.**—*Lancet.* 1936. June 6. p. 1290.

A suspension of leptospirae was made by mixing the sediment from about 250 cc. of Korthof's liquid medium with 10 cc. of meat broth (pH 7·6) to which was added 0·2 per cent. of formalin. The test was made by mixing various dilutions of the serum under examination with an equal volume of the leptospiral suspension and then keeping them for 2 hours at 52°C. Sera from 26 patients positive to ordinary agglutination and lysis tests were examined in this way and 25 of them gave a well marked agglutination that could be seen macroscopically.

E. H.

POT (A. W.) & DORNICKX (Ch. G. J.). **The Complement Fixation Test in the Diagnosis of Weil's Disease.**—*Jl. Path. & Bact.* 1936. Sept. Vol. 43. No. 2. pp. 367–372.

By using an improved antigen the authors have obtained good results in the diagnosis of Weil's disease and the reaction is reliable and easy in its performance and interpretation.

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* F.A.A. = formol, 5 ; acetic acid, 3 ; absolute alcohol, 46 ; distilled water, 46.

† F.A.S. = formol, 5 ; acetic acid, 3 ; saline solution, 92.

The antigen was prepared by centrifuging one week old cultures of leptospira in Korthof's medium for 3 or 4 hours at 3,000 r.p.m. The supernatant fluid is removed and the deposit suspended in 0·3 per cent. phenol saline in the proportion of 1 to 10.

A series of dilutions is mixed with (*a*) 1 : 100 dilution of an inactivated highly positive serum, and (*b*) 1 : 10 dilution of fresh guineapig serum, 0·3 cc. of each. After mixing the tubes are incubated at 37°C. for one hour and then 0·6 cc. of the haemolytic system added. The rack is incubated for 30 minutes and then the reading is taken.

When making tests two or three times this quantity is used and the dilution of serum which just gives complete inhibition is determined.

The results of the test were very satisfactory. 25 sera sent in for Wassermann testing were all negative ; 25 with a positive Widal gave one doubtful positive in a dilution of less than 1 : 10. The third group included 100 sera sent in for Weil's disease and were tested by the agglutination and lysis reaction as well as by complement deviation. Seventy-three of these were negative and of the remainder there was a satisfactory agreement in the results. In the case of 7 sera, however, agglutination or lysis occurred in dilutions of 1 : 30 and 1 : 100 whilst the complement tests were negative. None of these cases turned out to be Weil's disease.

The advantages of the complement fixation test over agglutination and lysis are mainly the fact that it can be performed by anyone accustomed to the Wassermann reaction ; the antigen is completely innocuous ; and there is an absence of the slightly positive tests that may lead to incorrect conclusions. *E. H.*

RAT-BITE FEVER.

WANSON (M.). Au sujet d'un cas de sodoku atypique observé au Congo Belge. [**An Atypical Case of Rat-Bite Fever in the Belgian Congo.**]—*Ann. Soc. Belge de Méd. Trop.* 1936. June 30. Vol. 16. No. 2. pp. 289–290.

The patient was bitten by a rat on the front of the left wrist ; the wound healed in a few days, but 15 days after the bite was inflicted the patient had a very painful swelling over the site and epitrochlear adenitis. Repeated examination of the blood yielded no spirilla, but a few were found in fluid obtained by puncture of the gland. Neosalvarsan brought about a rapid cure. The author records the case, first because he knows of no previous one in the Belgian Congo ; second, because at no time was there any rash seen, though the case was under observation for 18 days and the course of the fever was typical.

H. H. S.

RAMOND (Louis). Fièvre par morsure de rat "Sodoku." [**Rat-Bite Fever.**]—*Presse Méd.* 1936. Mar. 7. Vol. 44. No. 20. pp. 393–394.

A description of the clinical history of a case of sodoku, in which febrile symptoms developed only 4 days after the patient was bitten by a rat. *E. Hindle.*

SAIM (A.). Un cas de sodoku. [**A Case of Sodoku.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Bucarest.* 1936. Oct. Vol. 18. No. 8. pp. 235–237.

The description of the case of a patient who showed clinical symptoms of sodoku after being bitten by a rat. Parasites were not found, but the symptoms disappeared after injections of novarsenobenzol.

E. H.

IYER (M. A. Krishna). **Spirillum Fever caused by a Monkey Bite.**—*Indian Med. Gaz.* 1936. Aug. Vol. 71. No. 8. pp. 462–463.

A monkey ran " amok " and bit 22 persons of whom two developed a clinical condition exactly like rat-bite fever. The causative organism was not isolated, but the symptoms disappeared after treatment with neosalvarsan. *E. H.*

FRANCIS (Edward). **Rat-Bite Fever Spirochetes in Naturally Infected White Mice,** *Mus musculus.*—*Public Health Rep.* 1936. July 17. Vol. 51. No. 29. pp. 976–977.

The author calls attention to the fact that white mice may be naturally infected with *Spirillum minus,* and when using them for the diagnosis of rat-bite fever it is important to be sure that the mice are free from such infection, or preferably to use white rats or guineapigs. Examinations were made of the mice supplied to the National Institute of Health [U.S.A.] by 4 dealers. Three of them were supplying mice free from infection, but 45 out of 150 supplied by the fourth dealer showed spirilla in the peripheral circulation. *E. H.*

REVIEWS AND NOTICES.

MAXWELL (James L.) [M.D. Lond.]. **Leprosy. A Practical Text-Book for Use in China.**—109 pp. With 31 figs. (1 map). 1937. Shanghai, China: The Chinese Medical Association, 41 Tszepang Road. [4s.]

Dr. Maxwell has had an extensive experience of leprosy in China and has already contributed information on the incidence of the disease in that vast country. This book is intended for workers in China and to bring up to date the recently acquired knowledge of that disease. It commences with a historical account of the disease in China, where it was recognized as early as the sixth century B.C. and chaulmoogra oil was in use five hundred years ago. The chapter on incidence is illustrated by a map showing the highest rates in the Southern and Western provinces and in Shangtung in the North-east, without any relation to climatic conditions according to the author. The chapter on aetiology runs on orthodox lines with similar age and sex incidence to other countries.

The symptoms are well described, including the important early stages, and a number of good photos show the lesions in Chinese subjects. The author lays stress on the occurrence of nerve symptoms in all classes of cases.

Under pathology a few illustrations of sections of the skin are given, and lepra reactions are discussed, the author favouring their allergic nature in accordance with the views of WADE and RODRIGUEZ, and he also considers that the production of slight reactions during treatment with chaulmoogra derivates, including alepol intravenously, may be beneficial in stationary cases. In diagnosis the importance of the occurrence of nerve signs and finding the lepra bacillus microscopically are stressed. A chapter on types and classification follows the Philippine Conference suggestions, but it is pointed out that the portion based on microscopical characters of the lesions is not a practical one for such countries as China.

Under treatment the author is in agreement with E. MUIR, who is often quoted, in placing attention to the general health and removal of complicating diseases in the first place, to this he adds a good diet including adequate amounts of vitamins, such as can best be provided in China by soya bean and pea-nuts, and he urges the importance of calcium. He recognizes that chaulmoogra oil preparations form the best medicinal treatment by intradermal and other methods of administration, and also stresses their value in suitable early cases. After a short chapter on the difficult subject of prognosis, he concludes with an interesting one on Village clinics and Leper settlements, and urges the widespread use of the former in rural areas, where most leprosy originates, as the cheapest and most efficient prophylactic method. All through this small work the author reveals a clear grip of the subject, independent observation and facing of all the difficulties the disease presents. *L. Rogers.*

La Face (Lidia). **Fauna anofelinica delle colonie italiane.** [Anopheline Fauna of the Italian Colonies.]—*Riv. di Parassit.* Rome. 1937. Jan. Vol. 1. Suppl. Monogr. No. 1. 120 pp. With 29 plates. [73 refs.]

The value of this work to those who are not Italians is considerable, for it provides a full review of published information about the *Anopheles* of Italy's colonial empire, which falls into two groups, here distinguished as Libia and the East African possessions. For several of these countries it has been difficult for the ordinary person to obtain much information, particularly for such remote spots as Kufra and the Fezzan. The reader will observe with surprise that four species of *Anopheles*, including *A. superpictus*, have been collected in the Fezzan. All records are critically discussed, and several which are clearly based on erroneous identifications are rejected. The work appears to be thoroughly up to date in that it mentions species which have only recently been distinguished, and which are at present known only from other parts of Africa. It seems clear that in Italian East Africa, as elsewhere, the group of species resembling *A. funestus* will require much further study.

The rest of the monograph will no doubt prove valuable in the field, though it has no great interest for the general reader. In it the author summarizes the anatomy and classification of *Anopheles* and reviews the species which come on her list, treating some of them extremely shortly. Very little attention is given to biology or to the control of malaria. The bibliography might perhaps have had greater value if it had included more of the work which has been published on the mosquitoes of Tunis, Algeria, Palestine, etc. *P. A. Buxton.*

Swynnerton (C. F. M.) [Director, Tsetse Research Department, Tanganyika Territory]. **The Tsetse Flies of East Africa. A First Study of their Ecology, with a View to their Control.** With a Preface by the Right Hon. W. Ormsby-Gore, M.P., Secretary of State for the Colonies.—*Trans. Roy. Entom. Soc. of London.* 1936. Nov. Vol. 84. pp. xxxvi + 579. With 33 figs., 22 plates & 7 maps. [£5 10*s.* 0*d.*]

Mr. Swynnerton's book is prefaced by the Secretary of State for the Colonies, Mr. Ormsby-Gore, who calls attention to the general importance of what has been done, and makes fitting reference to the author's labours.

The body of the work deals with *Glossina* in Tanganyika Territory, much information being included about East Africa generally: indeed, relevant facts from West African sources have also been summarized, particularly where they relate to the widely distributed *G. morsitans*. For the most part the book is a summary, but it appears to contain some not yet published material about *G. morsitans* and *G. swynnertoni*. The first section of the text deals with matters of organization. After giving a brief survey of the general problem of infestation by *Glossina*, the author describes the gradual organization of his staff and the progress from the original survey to the time when reclamation as well as study became possible. One observes that the period of study lasted for roughly ten years, and that reclamation was seriously undertaken from 1931: but it is not clear whether reclamation then became possible

because of the progress of studies or because a large sum became available from the Colonial Development Fund. The author is, perhaps naturally, not very informative on the general question as to whether tsetse research should be carried out independently or attached to the medical or veterinary department of an African administration. The work is limited to the insects, little information being given about the local relation between fly and human or veterinary trypanosomiasis.

The author then gives a very full account of plant and animal communities in East Africa and of the species of fly which is characteristic of each of them. He then takes each species and discusses its biology in detail; these sections are very full, *G. morsitans* receiving 27 pages. Next follows an account of laboratory experiments, many of them carried out in West Africa, in which flies are kept subjected to controlled conditions of temperature and humidity. The author sees the value of such experiments, though fully aware of their artificial nature, and gives a critical discussion of their place in relation to field observations and to control. He then passes on to a full account of the food of *Glossina* in nature, a subject closely related to the control of game. This is followed by an account of natural enemies. Experiments on actual methods of killing *Glossina* form the subject of the next section of the work; there are a number of direct methods, such as the use of parasites, of hand catching, and of traps for adults and pupae, but the majority of the methods are indirect. Among them are mentioned the modification of woody vegetation so that it ceases to be attractive, or useful, to the fly. Here the author emphasizes the view that the wholesale clearing of thickets is not generally necessary, and that, indeed, it is often bad practice, for it is expensive and needlessly destructive. The view is put forward that clearing should be extremely localized, and also that it should be discriminative, being based on an exact knowledge of what the fly requires and of what are the least possible modifications that must be made in the environment. Clearing, however carefully carried out, requires to be supported by other measures; for instance, by proper timing of grass fires, or in other places by refraining entirely from burning the grass. Another indirect attack on fly is by way of the game; here also the author's point of view is critical and judicial. He admits that there are circumstances under which the killing of game may be valuable, but he states clearly that the value would be greater if we had a more precise knowledge of the game as a host for the fly.

Later sections of the work deal with practical matters. An account is given of methods of survey, including the use of air photography, and this is illustrated by a number of remarkable plates which show the distribution of the main types of vegetation on large areas of ground. The author also deals fully with the matter of reclamation. He remarks that Tanganyika has almost certainly spent more money on the study of control of *Glossina* than any other territory, and that it is relevant to ask what practical results have been obtained. The answer is set out in tables showing the areas cleared and the cost of the work. The reader is also given the history of the areas for several years after clearing. The author is able to record that successful work has been carried out which has stood the test of time, so that he and his colleagues may surely be congratulated on their achievements in that difficult sphere, where research leads on to practical measures in the field. The question of reclamation is particularly complex, because it is bound up

with the agricultural practice, anthropological and economic difficulties in human settlements, and the danger of erosion.

Lest the reader should think mistakenly that Mr. Swynnerton's book is a light one, it should be put on record that it contains 66 numerical tables in the text, 10 appendices and 22 plates and 7 large maps. Among the appendices we welcome particularly Dr. C. H. N. Jackson's account of the method by which he estimates the actual density of populations of *Glossina* in the field. This represents a great advance in the direction of precise quantitative work, for it is now possible to estimate the number of mature male flies in an area, though we cannot yet get any figure for the total number of flies of all ages and both sexes. We have already referred to the plates which show air photographs of different types of vegetation. The plate which shows the distribution of *Glossina* in Africa is perhaps a little imperfect in the north of Nigeria and the Gold Coast. The majority of the maps deal with distribution of vegetation, flies and reclamation. The last gives broadly the distribution of game animals in Tanganyika.

Mr. Swynnerton's book is hardly one which could be read in order to obtain a connected account of the subject. It might perhaps best be described as a large collection of facts and views, among which the reader might find what he required by referring to an elaborate table of contents which occupies 26 pages. We count it as a merit that the author is not dogmatic in his views and conclusions, and if the reader finds that the work is not very coherent he cannot blame the author alone, for it must be remembered that the subject is at present only partly developed. No one except Mr. Swynnerton could have produced so general an account of the natural history of tsetse flies in East Africa. Our thanks are due, not only to him and his colleagues, but also to the Royal Entomological Society of London, which has published this book with the assistance of a grant from public funds. *P. A. Buxton.*

MARTINDALE. **The Extra Pharmacopoeia.** Twenty-First Edition, in Two Volumes. Vol. 1. pp. xxxiv + 1182. 1936. London: The Pharmaceutical Press, Bloomsbury Square, W.C.1. [27*s*. 6*d*.]

For well over fifty years the "Extra Pharmacopoeia of Martindale and Westcott" has proved itself an essential source of reference on medicinal and pharmaceutical substances used in the treatment of disease. Following the death in 1933 of Dr. William Harrison Martindale, son of the William Martindale who first produced the "Extra Pharmacopoeia" in 1883, the responsibility for its continued production was assumed by the Council of the Pharmaceutical Society of Great Britain and, by their direction, volume I of the twenty-first edition now appears under the editorship of Mr. C. E. Corfield, who is also the editor of the British Pharmaceutical Codex.

This new edition has been completely revised, a large proportion of the material in it has been re-arranged and rewritten, and some out-of-date matter has been deleted to make room for useful accounts of the many new substances or modern applications that have been introduced since the previous edition appeared in 1932. Evidence of careful and thorough revision can be found throughout the volume; for example, in the much expanded notes on the use of totaquina,

plasmoquine and atebrin in malaria, and in the note on atebrin musonate, where reference is made to untoward effects, such as psychoses.

The major part of the volume is occupied by the materia medica alphabetically arranged, followed by sections relating to vaccines and sera, toxins and antitoxins, and to poisons and dangerous drugs. With its improved typography, its slightly larger format, and its carefully revised text and indices, this volume may justly claim " to continue to meet the need in medicine and in pharmacy of a comprehensive summary of the composition and application of the multitude of old and new, official and proprietary substances about which the doctor or the pharmacist may require information." *R. L. S.*

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